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Health Assessment of Occupational Exposure to Polybrominated Biphenyl (PBB) and Polybrominated Biphenyloxide (PBBO)

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HEALTH ASSESSMENT OF OCCUPATIONAL EXPOSURE TO POLYBROMINATED BIPHENYL (PBB) AND POLYBROMINATED BIPHENYLOXIDE (PBBO)

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ABSTRACT

The polybrominated biphenyls (PBBs) and polybrominated biphenyl oxides (PBBOs) are brominated hydrocarbons that have been used commercially as fire retardants. PBBs in particular are highly lipotropic and are not readily metabolized. As a result, they remain in adipose tissue for extended periods.

In August, 1978, a comprehensive medical evaluation was conducted on 42 out of 96 workers from a plant that manufactured decabromobiphenyl and decabromobiphenyl oxide and on 96 control workers from neighborhood industry not involving PBB. The exposed workers were employed in a plant that manufactured only brominated products and 96 regular employees worked there in the period January, 1973 to May, 1978. PBB serum level was significantly higher among the exposed group. An unexpectedly higher prevalence of primary hypothyroidism was found among the PBB workers than among the controls. Their sural sensory and peroneal motor velocities were significantly reduced when contrasted with controls. However, no significant dermatological, neurological or other adverse health effects were clinically demonstrated.

HEALTH ASSESSMENT OF OCCUPATIONAL EXPOSURE TO POLYBROMINATED BIPHENYL (PBB) AND POLYBROMINATED BIPHENYLOXIDE (PBBO)

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INTRODUCTION

Brominated aromatic hydrocarbon compounds manufactured for use as flame retardants have been recognized in the last decade as a potential source of environmental contamination.[1] Polybrominated biphenyls (PBBs) and congeners have a close structural relationship to the widely prevalent polychlorinated biphenyls (PCBs). PBB is a highly lipotropic substance that is not easily metabolized or biodegraded.[2] As a result, PBB remains in human adipose tissue and in the general biosphere for extended periods of time. Polybrominated biphenyl oxide (PBBO), an ether, is less inert and slightly more readily metabolized than PBB. PBBO is still very stable, because the oxygen bonds are not easily broken.

PBBs have not been associated with cancer in humans. This may be due to the fact that PBB manufacture first began in 1970.[3] Both PBB and PCB have been associated with the development of neoplastic liver nodules in rats.[4] A possible relationship between PCB and cancer in humans was noted in a small cohort of workers.[5]

Following the accidental contamination of dairy cattle feed in Michigan in 1973 by the fire retardant BP-6 Fire Master, principally a hexabromobiphenyl, animals showed anorexia, hair loss, skin roughening, abnormal hoof growth, liver abnormalities, decline in milk production, loss of weight and death.[6] An increase in stillborn and malformed calves also was seen.[7] Animal experiments with PBB and related substances have demonstrated thyroid and liver changes, infertility, retardation of intrauterine growth and other fetal effects.[8-13] The symptoms of possible PBB-related illnesses reported in humans who consumed the contaminated animal product included muscle pains, fatique, weaknesses and sleep disorders, skin, neurologic and gastrointestinal difficulties and immune dysfunction.[14-16]

The effects on human health of exposure to PBB have been studied in quarantined farm residents, consumers of farm products, chemical workers (from Michigan) and in a control group of farmers from Wisconsin. Differences in symptoms were found between exposed and nonexposed groups; however, symptom prevalence rates had no consistent relationship to body burdens of PBB as measured in serum or in adipose tissues.[17-18] No consistent differences in objectively measured variables between exposed and nonexposed individuals have been reported. Results of studies on immune dysfunction, for example, have been conflicting.[18-19]

PBBs, specifically the octa- and decabromobiphenyls, have been found in the environment (soil, water, sludge) around the sites of certain major producers.[20] While there is concern with the effects of PBBs on the general community, workers engaged in their manufacture may have had an earlier exposure to higher concentrations than the community; therefore, health effects can best be elucidated in workers as the first approach to risk assessment in man. Workers engaged primarily in the manufacture of PBB would appear to represent the ideal study group. Accordingly, a cohort of workers in a plant engaged in the manufacture of decabromobiphenyl was identified, and a sample of these workers was examined in August, 1978.

METHOD

The major objectives for the health effects study were as follows:

(1) to measure the extent of worker exposure to PBB;
(2) to determine if associations exist between certain adverse health effects and exposure to PBB;
(3) to identify early indicators of adverse health effects as associated with exposure to PBB;
(4) to compare current health status with preexisting health conditions and to identify other toxic exposures in order to assist in evaluating which conditions may be the result of exposure to PBB.

To fulfill the above objectives, the study was designed to:

(i) maximize comparability of the data collected with data from other human and animal studies of exposure to PBB;
(ii) examine effects of other toxic substances at work and at home;
(iii) permit adjustment for age as a known/suspected covariate in adverse health conditions;
(iv) take into consideration other demographic characteristics, health conditions and life style prior to, during, and after exposure to PBB.

THE STUDY POPULATION

a) Exposed Workers

The approach to the epidemiological investigation of PBB-induced health impairments involved both current and past workers. This appeared to maximize the research potential because subjects are not drawn only from those currently employed at the facility. The enlarged sample included those workers who may have been hospitalized or who quit their jobs as a result of intolerance to exposure in the workplace.

The company chosen for the study specialized in the production of brominated chemicals. Approximately 200 workers had been employed at the plant between January 1, 1973 to March 31, 1977, during which decabromobiphenyl (PBB) was manufactured. Since then, decabromobiphenyl oxide (PBBO) has been the major manufactured product. This plant was selected for study because 1) it had only manufactured brominated products which minimized the possibility of potentially confounding industrial chemical exposures, and 2) a high degree of cooperation between the investigators and management existed which was an especially important consideration since the plant is not unionized.

A total of 92* workers (excluding 4 known deceased) were employed at the plant for at least 6 weeks (or 240 hours) between January 1, 1973 and May, 1978. These workers were contacted by registered mail with the assistance of the company.

b) Control

It was determined that the control groups should consist principally of blue collar workers employed in the same community thus controlling for socio-environmental factors. The study would be conducted in a double-blind fashion. It was also desirable to draw the comparison groups from other industries in order to control for the possibility of unforeseen health effects specific to a given industry. Furthermore, the relatively small size of the PBB worker cohort suggested the need for a larger control population.

For each person in the PBB worker cohort, it was planned that one control worker would be matched from each of two selected industrial groups by sex, race and age (± 5 years). Those used were the 1) local steel workers and 2) electricians. It should be noted that other groups who were unlikely to have been exposed to any chemical also had been approached. However, factors pertaining to scheduling and employer cooperation resulted in the inability to use other industrial groups for control purposes. A supplemental group was examined on-site and included to complete the age-matched triads.

QUESTIONNAIRE

The interview questionnaires were constructed to obtain the maximum information within the time available. Where possible, items from standardized questionnaires were utilized. Content, format, and language were selected to reduce ambiguity and elicit maximum response rates. Internal checks on the reliability of key items included the duplication of some questions in different portions of the questionnaires. Thus, questions pertaining to exposure to chemicals, fumes and dust were asked in an open-ended format in the lifetime occupational history as well as in the closed format. The latter check list of specific toxins was asked after the occupational history had been taken.

*Following completion of the field study, two workers were declard ineligible because they did not meet the criterion for the period of employment. The cause of death is shown in Table XIV.

Validity (true positivity) was enhanced by obtaining information on symptoms that were moderately severe and of long duration. Also information was requested for: (1) dates and names of physicians who were seen for conditions or who prescribed medications and (2) dates of all hospitalizations including names of hospitals and reasons for hospitalization.

Presented below are the items contained in each instrument:

a. Demographic-occupational-smoking-drinking questionnaire

1. Age, race, sex
2. Educational attainment
3. Places of residence since 1972
4. Lifetime occupational history; specific chemical, dust and fume exposures, by duration and type of contact (e.g., inhalation, skin)
5. Avocational contacts with chemicals, dust and fumes, by frequency and duration of contact
6. Smoking history
7. History of alcohol and "street" drug usage.

b. Medical history questionnaire

1. Name/address of personal physician
2. Self-rating of overall health and change in health over time
3. History of hospitalizations including admission date, length of stay, name/address of hospital, presenting problem and current status of problem
4. History of physician-diagnosed medical conditions by system, including date of original diagnosis, attending physician, status of condition, prescribed medication(s)
5. Symptom review (over last five-year period) by system including dates of occurrence, physician contact and current status
6. Supplementary dermatological symptom and medical history
7. Supplementary respiratory symptom and medical history (based on the Medical Research Council Schedule)
8. History of medication(s) usage by drug type, including specific drug, dates of usage and prescribing physician.

PHYSICAL EXAMINATIONS

a) General Physical Examination

This examination consisted of observations on general appearance, head, eyes (non-fundoscopic), neck (thyroid), lungs, abdomen, genitalia, lymph nodes, joints. Measurements of blood pressure, pulse, height, and weight were taken.

b. Dermatologic Examination

Like other halogenated aromatic hydrocarbons, PBB is stored in the sebaceous glands of the hair follicles. Exposure to this substance may cause haloacne dermatitis, palpebral swelling and ocular discharge, and other dermatologic conditions. To assure that no adverse dermatologic effects would be missed, a consultant dermatologist was employed to examine all screenees. He recorded his results on a form modified after Selikoff.[21]

c. Neurologic Examination

The reports from the Michigan PBB studies indicated the occurrence of health effects such as fatigue, sleep problems, personality change, lack of coordination, and other ill-defined central nervous system manifestations (11,14,15,22-29). Hence a consultant neurologist was employed to conduct a neurologic examination of the cranial nerves, reflexes including abnormal reflexes, and to test motor coordination. In addition, the neurologist administered a standardized "mini-mental status" examination developed by Folstein and McHugh (University of Oregon).

d. Nerve Conduction Test

A major decision concerned how to measure in the field any possible early damage to peripheral nerves. To test clinically suspected neuropathy, conduction studies involving the insertion of special needles constitute a more reliable and valid procedure. Neurologic experts agreed, however, that under field conditions and as a screening examination, the use of surface-electrodes to measure amplitude and velocity of nerve conduction would be adequate. Furthermore, it would have been difficult to justify any invasive procedure without evidence of neuropathy, and such a procedure might have lowered the participation rate.

A portable instrument was used to study the following nerves: peroneal motor, sural sensory, ulnar sensory, median motor and median sensory.

LABORATORY TESTS

a. Markers of Amount of Chemical Exposure - Serum PBB, PBBO and PCB Levels

Because of its lipotropism, the best indicator of PBB exposure is the level of PBB in adipose tissue. However, obtaining a fat specimen requires an invasive procedure (needle aspiration or incision). Such a procedure could not be justified at this time for the following reasons: serious health effects to PBB had not yet been demonstrated in this population; under field conditions, an operative procedure would be difficult as well as costly; the participation rate of PBB workers would suffer and the procedure would be unwarranted for non-PBB workers.

A strong correlation (r = 0.98) was found between fat and serum PBB at detectable levels in the serum (40% of the Michigan sample).[30] Therefore, it was decided to assay serum for levels of PBB. At the same time, serum levels of PBBO and PCB would be routinely assayed.

b. Urine Tests of Liver Microsomal Enzyme Induction

PBB and related compounds have been reported to induce a number of microsomal enzymes in the liver and other organs.[31] Induction of two major enzymes, UDP-glucuronyltransferase and hepatic cytochrome P-450, can be measured by increases in porphyrins and glucaric acid in the urine. The specific measures of porphyrin metabolism tested were: total porphyrins (copro- and uro-), porphobilinogen, delta aminolevulinic acid (ΔALA). Creatinine levels were recorded as well.

Because of the possibility of diurnal variation, optimal measurement is made from 24-hour urine specimens. There were several deterrents to routine 24-hour urine collection in this field study: (1) confidentiality of worker participation in the study prevented urine storage during the working day at the PBB plant; (2) half of the PBB cohort were former workers; both this group and the electricians worked at a variety of sites; (3) some screenees arranged appointments the day before the examination.

Arguments in favor of spot urine collections were: (1) NIOSH reported (personal communication) that standardized (normal) spot urine porphyrin/creatinine ratios did not indicate marked diurnal variation; (2) It has been shown that glucaric acid/creatinine ratios derived from spot urines correlated with ratios derived from 24-hour urines,[31] 3) Group comparisons of PBB workers and controls would be made.

The compromise decision, therefore, was to collect spot urines from all subjects during the examination (the amount of urine augmented by ingestion of non-caffeinated sugar-free beverages) and to encourage the collection of 24-hour urine, either before or after the examination, by payment of an additional participation fee.

c. Other Tests of Effects on the Liver and Fat Metabolism

Liver damage such as liver enlargement and fatty swelling was reported to be associated with PBB exposure; however, no laboratory tests specific to effects of PBB as differentiated from excess alcohol or other toxins could be identified. Therefore, standard laboratory measurements of liver functions were carried out: LDH, SGOT, SGPT, YGT, bilirubin, alkaline phosphates. In addition, questions were asked about history of jaundice and the size of liver was noted at the examination.

PBB is also reported to induce hyperlipidemia. While both serum cholesterol and triglycerides were measured, the triglyceride value in particular is not valid since it was not feasible to obtain a 14-hour fasting blood specimen. (A two-hour preexamination fast was requested, however.)

d. Tests of Infertility

Damage to the interstitium (Leydig cells) of the seminiferous tubules is manifested by impaired maturation of the spermatocytes. As a result, a decrease in the sperm count will occur before levels of testosterone, LH or FSH are significantly affected. Collection of sperm samples was not considered feasible for the following reasons: (1) practical difficulties in collecting sperm samples on site (personal communication, University of Illinois study of the workers); (2) sperm specimens could not readily be brought to the examination site by workers coming directly from work; (3) required abstinence from sexual intercourse for at least 48 hours prior to examination might deter participation; (4) sperm counts are extremely variable, necessitating at least two specimens to confirm impaired fertility and (5) under field conditions, only sperm count and sperm anatomy could be determined but not sperm motility from specimens.

Since a below average testosterone level found in a preliminary study provided some cause for concern,[32] serum levels of LH, FSH and testosterone were measured. Additional information on fertility was collected: inspection of testes for evidence of atrophy; a fertility history of the workers was taken; and a detailed reproductive history was planned for their wives at a later date.

e. Thyroid Function Studies

To measure thyroid function, the following tests were planned for each screenee: T_4, resin T_3 uptake, TSH. T_3 levels were measured when hyperthyroidism was indicated and serum thyroid auto-antibodies assayed when hypothyroidism was found. Also, the thyroid was examined and symptoms of thyroid dysfunction ascertained.

f. Miscellaneous Laboratory Tests

Routine hematology and an SMA-24 screen were done to detect a wide range of biochemical abnormalities.

g. Reliability Control

To test reliability, a 10% random sample of all values and of certain abnormal values was independently re-assayed. (Frozen serum is stored at the University of Pennsylvania and at Research Triangle Institute, Inc., in the event that additional tests are justified.)

h. Procedures

Table 1 in the Appendix summarizes the laboratory procedures.

DESIGN OF THE FIELD STUDY

a. Exposed Cohort Group

A coded list of all 32 former and current PBB workers employed since 1973 for a minimum period of 6 weeks (or 240 hours), as of May 1978, was furnished by the company. The company had stipulated that it could not release the names of employees without individual consent. Therefore, the furnished list omitted actual names and contained only cohort number, date of birth, employment starting date, termination date (if not currently employed) and job classification. To meet confidentiality requirements, the company sent, by certified mail, letters to all workers on the cohort list with the provision that mail receipts, deleting identifying information but substituting cohort list number, be shown to the University of Pennsylvania. Letters to twelve cohort members were stated to be stamped "undeliverable".

Cohort members were sent a letter which briefly described the health effects study and outlined the types of medical examinations and tests to be performed noting possible risks. It assured confidentiality in handling data obtained and the right of the participant to withdraw from the study at any time. Workers were informed of the time and location of the study and of the compensation coverage and amount. Phone numbers of the Principal Investigator (with reverse charges) as well as of a local nurse (R.N.) were provided.

A detachable Informed Consent Form provided several options for participation: (1) medical examination (with knowledge by the company) and authorization to release company work and medical records; (2) medical examination but without authorization to obtain company held records; and (3) agreement for release of company records but without participation in the medical examination. If the worker did not wish to participate, no reply was requested. A stamped envelope addressed to the Principal Investigator was enclosed for returning the signed Informed Consent.

Prior to this mailing, all consent forms were numbered to correspond to the cohort list number, enabling a later comparison between respondents and non-respondents. Upon receipt of the consent form by the Principal Investigator, the nurse contacted the worker by telephone and arranged for an examination appointment. She used a standardized telephone format and scheduled appointments on a random basis.

The week before the examinations, a second mailing (non-registered mail) was sent by the company to all members of the cohort to recruit additional participants.

b. Comparisons

The general procedures outlined above also pertain to the enlistment of the controls except for some modifications. For one control group, a membership roster was provided by a local electrical workers union. The 103 members were

sent a letter directly from the Principal Investigator by regular mail. The detachable consent form did not include the options for the release of company work and medical records. Before scheduling appointments, the nurse queried workers as to whether they were wiremen or linemen; the latter group was excluded from participation because of hypothesized exposure to PCBs used in large capacitors or transformer coolants.

The steel workers were contacted by union representatives. Agreement to distribute letters and consent forms was obtained at a local union meeting, attended by the University of Pennsylvania staff.

Additional controls were recruited by personal contact at a county planning board and similar procedures.

c. Procedures to Maximize Participation

The field study was planned to assure maximum participation. The scheduling of appointments was flexible; early morning, daytime and evening hours could accommodate diverse scheduling requirements. As stated, invasive, uncomfortable and excessively inconvenient laboratory procedures were eliminated from the study (e.g., obtaining sperm and adipose specimens, etc.). Inducements for participation included monetary incentives, ($25* plus travel expenses, with an additional sum of $5 offered for 24-hour urine collection), the opportunity to learn about their own health and to participate in a significant research endeavor. Furthermore, the participants could decide the extent of their involvement (University access to company-held records, donation of 24-hour urine specimens, etc.). Finally, the site selected for conducting the study was convenient, accessible, and neutral.

d. Protection of Subjects' Rights and Right to Information

The principles of informed consent and confidentiality and the subject's access to his examination results were strictly followed.

e. Special Procedures for Avoiding Bias in the Study

To minimize possible bias, the study was conducted without any publicity and with concurrent controls. The following precautions were taken to reduce potential bias resulting from knowledge of PBB exposure or its effects:

a. Statements to PBB workers and control workers described the investigation only as a study of health effects of various occupations in the area.

b. Controls were chosen from the same local area so that they could participate in the same manner as the PBB workers; i.e., concurrent controls.

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*Subsequently, the company announced to current workers that an additional $25 would be provided to participants (all payments were made by the University to protect confidentiality).

c. Appointments were scheduled in a generally random order using a standardized telephone format; workers were interviewed and examined in the same type of white gown; workers were informed verbally and in writing not to divulge their occupation except in the demographic interview; medical history interviewers were instructed not to inquire about occupation, medical history or symptoms; and all phases of the interviews and examinations were conducted by different individuals.

f. Training of Interviewers

The team of interviewers consisted of two medical students, four graduate students in epidemiology, one nurse (R.N.) and one graduate student in journalism.

These interviewers received specialized training in the administration of either the medical history or the demographic questionnaire based upon their educational background and experience.

They participated in two training sessions. The second training session was conducted at the actual site the day prior to the actual interviews and examinations. Interviewers reviewed the final questionnaires and role-played the respondent, alternating interviewer and respondent roles.

Interviews and examinations were conducted during the last week of August 1978, at the Parish Center. This site was selected because of its proximity to the PBB plant and its familiarity to the community. The physical layout provided ample, well-defined space for conducting the separate examinations, tests and interviews. Figure 1 shows the first floor of the center, indicating the location of each examining/testing station.

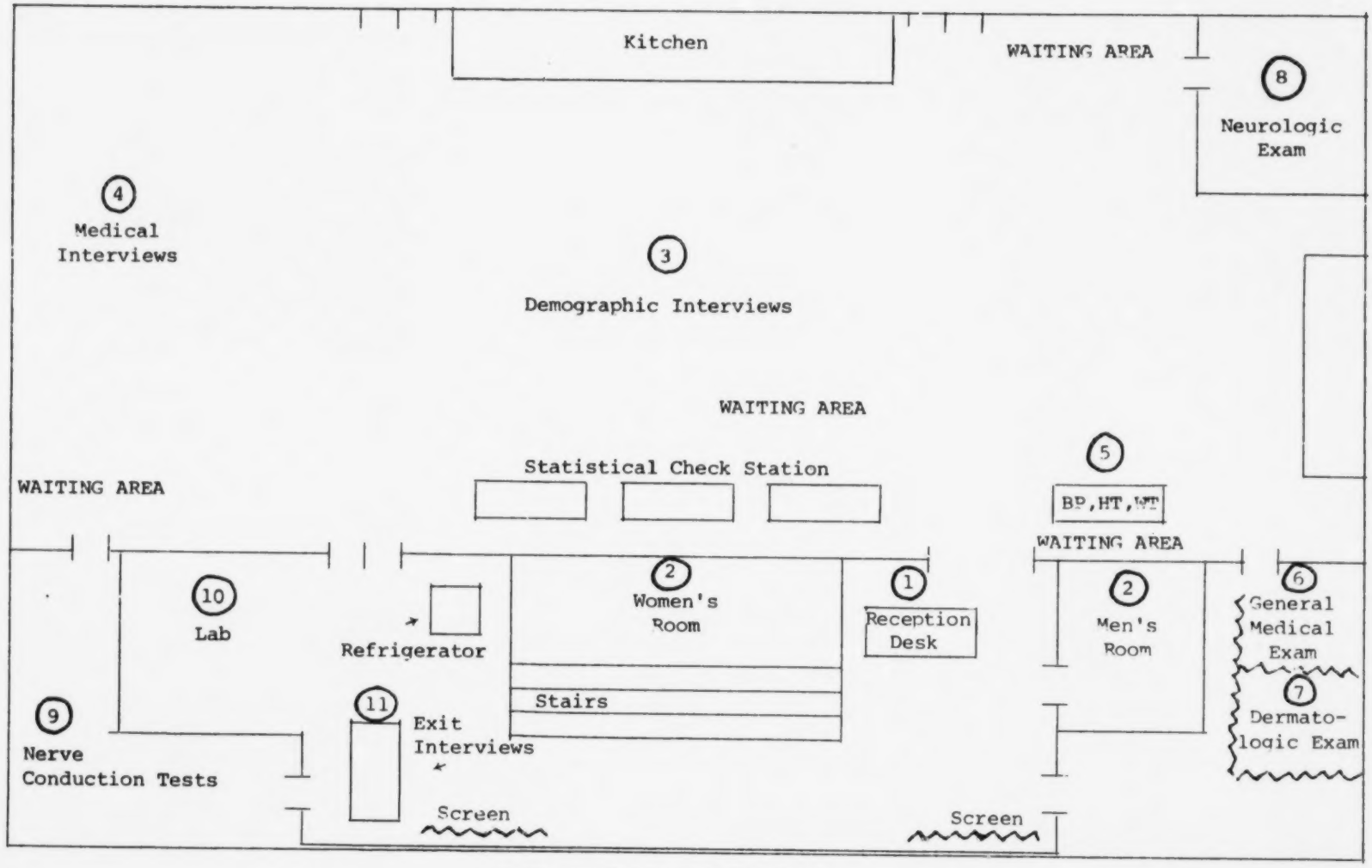
g. Conduct of the Field Study

Participants first checked into the reception area where they were greeted, "logged in" on a roster log sheet, and the completion of their consent forms verified. Participants were then given a general description of the procedure to be followed and handed their master folder. This folder contained all interview and examination forms (each differently colored and lettered), consent forms for the nerve conduction examination, and permission for examining specified records. A control sheet was stapled to the face of the envelope.

All material in the folder was prenumbered with the ID (serial) number of the screenee. Four detachable labels with ID number and the screenee's initials were also provided. The first label was placed on the examinee's gown to assure correct matching with the forms, the second on the refrigerated urine bottle, the third on an empty folder given to a Control Station and the fourth given to a clerk for preparation of labels for laboratory tests. The master folder was carried by the interviewee throughout the examination-interview and "emptied" of its contents at the appropriate stations.

FIGURE 1.

Floor Plan of Parish Hall



After checking in at the reception station, the screenees went to a dressing room area where he/she changed into an examination gown and gave a urine specimen. Subsequent assignment to a particular station proceeded on a random rather than a predesigned, sequential basis. This was necessitated by the variable length of time required to administer the demographic and medical history questionnaires. For each phase of the study, the initials of the staff interviewer/examiner responsible and time (in and out) were noted on the Control Sheet affixed to the screenee's folder. In this way, phases yet to be completed by the screenee could be readily determined. All completed forms were taken by the staff to the statistical check station where they were reviewed for completion and assembled in the code-numbered empty folders.

Prior to leaving the examination area, screenees were asked to give their final urine specimen and to participate in an exit interview which consisted of a second check that all phases had been completed; "debriefing"; the signing of authorizations for obtaining medical records and consent to give a 24-hour urine (if not already done), and the payment of participation fee and travel expenses.

h. Post-field Debriefing

On September 12, 1978, project staff met with the field interviewers to evaluate: a) quality of interviewing process; b) congruence between written protocols and actual process in order to adjust for any noted deviations; and c) extent to which any alteration in procedures might have produced biases in information collected.

Based on the reports of the interviewers, it is believed that there was a high degree of congruence between their activities and planned procedures. It appeared that problems encountered in the field (e.g., scheduling) did not influence in any significant direction or degree the interviewing process itself. Additionally, a high degree of rapport between the interviewers was reported by the latter. These findings, corroborated by a nationally recognized consultant's on-site report and comments of individual screenees to the Principal Investigator, enable project staff to have confidence in the "face" validity of the information obtained during the interview phase.

i. Data Processing

As in the field study, the same concern for "blinding" was followed in all data processing phases. Discrete duties were assigned to different individuals to minimize any opportunity for decoding employment status. Thus one individual worked only with workers' permissions and copies of company-held work and health records. The questionnaire/instruments and laboratory reports were coded without reference to employment status, with the exception of the demographic occupational questionnaire which provides employment information for coding. Prior to any statistical analysis, data were cleaned from punching and transcription errors. All laboratory values were assayed in coded form and their transcription doubly checked.

j. Publicity

Since this study had almost been aborted by the quoted statement of the then EPA Project Officer on January 17, 1978 to the local newspaper that "suggestive evidence" exists that PBBs are carcinogenic, special efforts were made to insure that all further publicity was minimized and all press relations were handled through the University.

METHOD OF ANALYSIS

The analysis began with a general description of each of the tested variables for the total study population. This preliminary phase was important for the determination of the overall distribution of the variables and identification of outliers. It was then possible to determine the required transformation necessary to permit application of linear models techniques or to demonstrate the need for the application of non-parametric tests of significance. From examination of the distributions, a number of laboratory tests were found to be skewed to the right; a logarithmic transformation was made to improve normality.

Appendix Table II lists the "normal" ranges of all laboratory test values given by the laboratory or the literature. This table also gives the mean, the standard deviation and corresponding range for 95 percent of the study population means. It is evident that in a few laboratory tests, (e.g., leucocytes), the normal ranges as reported in the medical literature vary from the 95 percent range found in our study. This deviation can be explained by either some variation in the laboratory techniques or the effect of handling the specimens during the phases of the study. However, it is expected that the samples were handled in the same manner in both the PBB exposed group and the comparison controls. As a result, any statistical comparison described is believed to be valid.

One hundred and thirty-eight workers participated in the study: 42 PBB workers, 42 electricians, 26 steel workers and 28 others. It was planned that all PBB workers would be matched by age group, race and sex with the workers from the comparison groups. However, under field conditions, it was not possible to "control" for age (e.g., not all persons who made appointments came in for an examination). The electricians, in general, were older and the steel workers younger than the subject group. Therefore, since many of the biological variables studies are age-related, age matched triads were formed for males (Appendix Table III). In forming the triads, 28 of the PBB workers were matched ($\pm$ 5 years) with the electricians and the 8 youngest PBB workers were matched with workers from the "other" group. All 25 steel workers were matched with the PBB workers; the remaining 11 PBB workers were matched with workers from the "other groups". Except for matching by nearest age and occupational group, selection was made without examination of other characteristics of the individual.

In the preliminary analysis, the study population was grouped in five ways:

1. the total population (138) of examinees

2. by triads - 36 male PBB workers matched by age and race to controls (electricians and others, steel workers and others) (see Table IV)

3. by sex and employment

   i. 39 PBB workers (36 males, 3 females)
   ii. 26 steel workers (25 males, 1 female)
   iii. 42 electricians (42 males, no females)
   iv. 28 others (24 males, 4 females)

3'. as (3) with medical exclusions (alcoholism, diabetes, etc.)

4. by PBB male workers versus all other male controls (36 PBB workers vs. 91 controls)

4'. as (4) with exclusions as in 3'

5. by triads, sex and race (10 groups)

i.	A	34	- PBB workers, white males only
ii.	B	34	- electricians and others, age-matched with A
iii.	C	34	- steel workers and others, age-matched with A
iv.	F1	3	- PBB workers, females
v.	F2	5	- control females
vi.	MM1	2	- PBB workers, non-white males (1 black, 1 other minority)
vii.	MM2	2	- non-PBB workers, non-white males (1 black, 1 American Indian)
viii.	EX1	16	- unmatched electricians
ix.	EX2	5	- unmatched others
x.	EX3	3	- ex-PBB workers who were classified as ineligible.

One-way analysis of variance tests (ANOVA) using BMDP7D[33] identified significant differences with respect to laboratory values between the exposed groups and the comparison groups (unadjusted for the effects of other exposures). The following points are noted:

a. A one-way ANOVA among the triad matched groups can be considered as an analysis of covariance, where age was controlled as a covariate, without actually estimating the age effect. The BMDP7D program also provided a detailed description of each of the biological variates, i.e., histograms, means, standard deviations and ranges within each group as well as for the total study population.

b. ANOVA among the four groups as defined in (3) above was appropriate since it was expected that the "other" group might "contaminate" either the electricians or the steel workers, and as a result, existing differences would not be identified. By applying such methods, it was assumed that age had a negligible effect on the variates studied.

c. Applying the BMDP7D program to the 10 subgroups, as defined in (5) above, was necessary for completeness.

d. The editing procedure pointed out variables with non-normal distributions. In such cases the comparison among groups was carried out by applying the logarithmic transformation prior to the ANOVA. These variables are indicated with "*" in Appendix Table II. No transformation normalized truncated distributions such as the TSH assays. In those cases, non-parametric methods (i.e., χ^2 test) were substituted for the ANOVA test.

e. Special analyses were performed for the nerve conduction studies. It was not feasible to maintain age matched traids following the exclusion of all subjects with known extraneous causes for neuropathy (which resulted in the groupings 3' and 4' above). The analysis of covariance was an appropriate post hoc procedure by which to adjust for possible bias introduced by the unequal age distributions which resulted. Assumptions which must be met in order that the procedure by valid were examined, utilizing P-P plots[34] and the exploratory data analysis techniques due to Tukey.[35] The choice of an appropriate transformation must be determined with primary consideration given to the form of the functional associations of each nerve conduction response with various covariates, e.g., age, heavy metals and solvent exposures, the PBB blood serum levels and, for the workers, measures of occupational exposure to PBB such as length of employment at the plant. Techniques which examined, in order to improve, the applicability of the classical multiple linear model for the analyses of these variables were implemented subsequent to the preliminary analysis reported here. Further consideration of appropriate transformations for the peroneal motor, median motor and median sensory velocities remained to be made and are to appear in a separate paper.

The above methods apply to quantitative variables. Qualitative variables were analyzed by chi-square tests. In the detailed analysis of thyroid function data, the Z test, Fisher's Exact Test and the Mann Whitney Test were employed.

In summary, investigation began with the description of the sampling distributions of measured variables for the study as a whole. For the quantitative laboratory variates, analysis of variance F statistics were examined to determine if there were significant differences across the following selections for groups: (2) the triads, (3) by employment (PBB, steel workers, electricians and others), and (4) by PBB workers and all controls taken together. The major comparison presented here will be for the matched triads, (2). Further preliminary study of the nerve conduction velocities included analyses across groups defined by employment (3') with adjustment for age using an analysis of covariance model.

For the comparisons across triads, ANOVA F statistics, testing the overall adequacy of the model to explain the variation in the responses, are reported with the P-values appropriate to two-sided tests. An $\alpha = .05$ level of significance would be consistent with standard practice in assessing the reported P-values. For the laboratory variates, no attempt at contrasting specific controls with the PBB group was made, and thus no determination of simultaneous testing levels (with an overall α level of protection) was necessary.

However, for nerve conduction studies, reduced velocities were the only alternatives possible. Thus, one-sided tests for contrasts of PBB workers with controls were indicated and P-values (indicated by P^*) appropriate to one-sided tests are given. No overall, or simultaneous α-levels are attempted for these contrasts in this exploratory investigation.

It should be noted that in addition to the contracted computer analysis, a physician reviewed selected portions of the questionnaires, e.g., symptoms, and the results of the physical, dermatological and other examinations.

RESULTS

a. Demographic and Occupational Characteristics

One hundred thirty-eight workers participated in the field study:

42 PBB workers: 34 white males, 2 non-white males and 3 females

(3 white males were ineligible for the study based on employment data and 1 worker who participated was not on the original cohort list)

42 electricians: 42 males

26 steel workers: 23 white males, 2 non-white males and 1 female

28 others: 24 males and 4 females.

The 39 PBB eligible workers represent approximately 45 percent of both current and former workers who were employed by the company for at least six weeks during the study period (January 1973 - August 1978). The study included 3 female workers employed by the company from 1972 - 1975, 1965 - 1978, and 1975 - 1978. Because of their small number, the characteristics of the women are described separately. Figure 2 documents period of employment for the 36 PBB male workers.

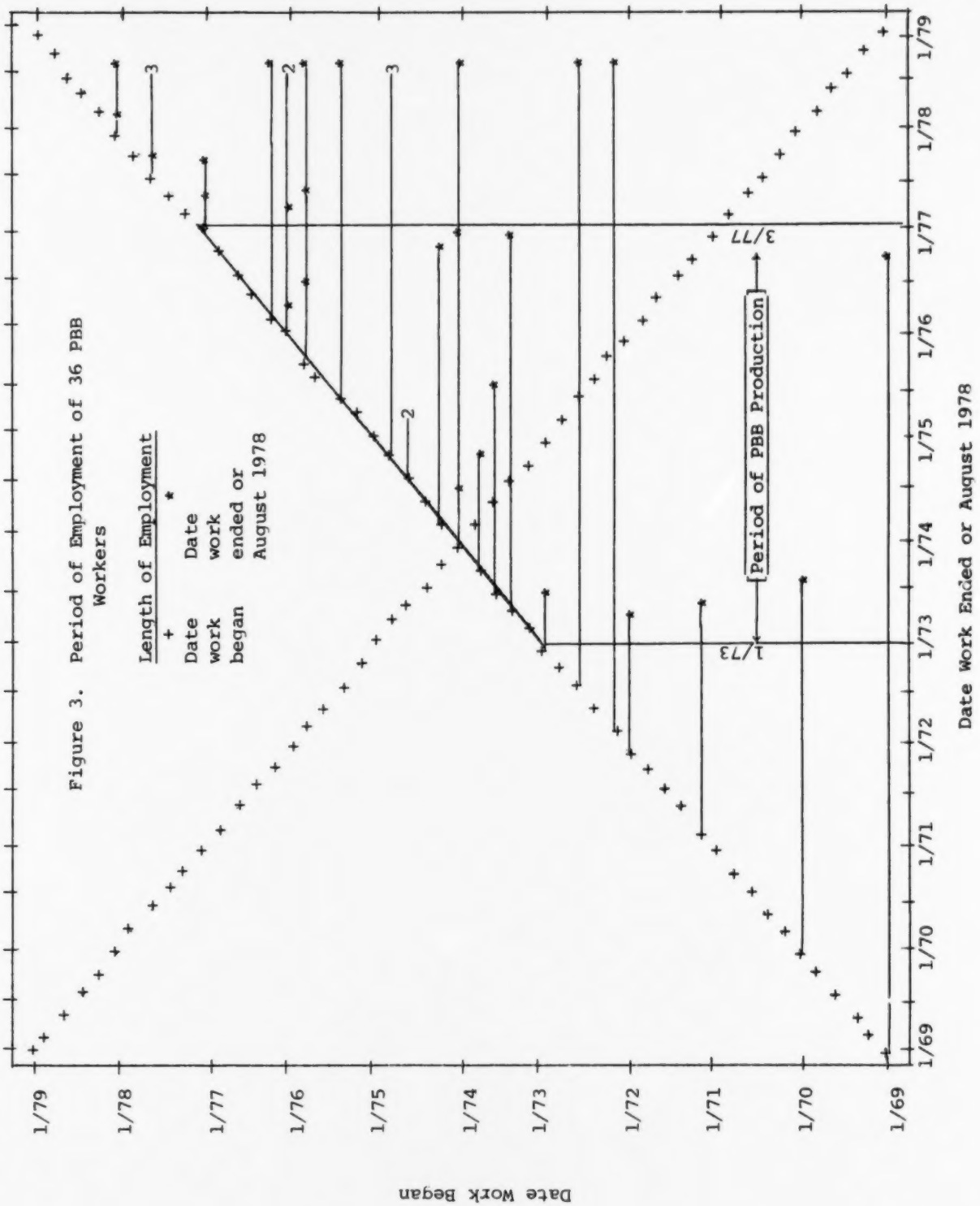
The median age of the 36 PBB males was 30 years (range 22 to 57 years). PBB workers did not differ significantly in age from the entire male cohort.

The mean duration of total employment (27 months) and of employment during PBB production for the PBB workers (19 months) (Figure 2) did not differ significantly from that of the entire male cohort. (z value for total duration of employment: -.644; z value for employment during PBB production: .058.)

b. Medical History

The frequency of reported symptoms "any time during the last five years" by system and occupational group (Appendix Table V) indicated no statistically signficant difference in comparing the entire three major occupational groups.

Figure 2. Period of Employment of 36 PBB Worker/Examinees (Males)



c. Physical Examination

Two PBB workers and one electrician had an enlarged liver (defined as >13 cm. total or 2 cm. below the right costal margin). Review of the medical histories of these men revealed no indication of antecedent liver disease. All three had at least one elevated liver enzyme test. Of these, only one person (PBB worker) had a history of heavy drinking.

d. Dermatologic Examination

The data were reviewed for any evidence of haloacne dermatitis. Active acne, or scarring resulting from a prior acne condition was evidenced in 69.2 percent of the PBB workers, 65.4 percent of steel workers, and 76.2 percent of electricians. The difference is not statistically significant.

e. Neurologic Examination

Neurological problems were clinically identified in only a few workers in the study. Comparison of the four groups (PBB workers, electricians, steel workers and others) showed no statistically significant difference (see Table VI). No abnormal motor and coordination behavior or abnormal mental state was demonstrated by the "Mini-Mental Status" examination.

f. Laboratory Tests

The mean values of the quantitative variables studied are presented in Appendix Table VII. The percentage distributions of laboratory values, defined as above-normal, normal, and below-normal as found in the matched triads are presented in Appendix Table VIII. Abnormal results were defined by the laboratory or the literature when such data were not available, e.g., spot urine values. A "normal range" was determined for the study based on the marginal distribution of the study population. Improper collection or storage of some specimens may have resulted in some of the abnormal values.

1. Hematology

No statistically significant differences were found in the three age-matched groups using analysis of variance techniques (Appendix Table VII). The laboratory normal range differed from the 95 percent value for a number of these variables (e.g., LDH) (Appendix Table II).

2. Blood Chemistry

A statistically significant difference in the mean for the three groups was shown for serum phosphorous (P=0.03) (Table VII). Statistically significant (P=0.03) negative correlation between length of employment at the PBB factory and particular serum levels (e.g., total protein and serum triglyceride) was found (Appendix Table X). The findings of high serum phosphorus in electrical workers and of a negative correlation between period of employment and total protein and triglycerides may be interpreted as chance associations until additional supportive information is provided.

3. Urine

Appendix Table IX indicates that the qualitative tests on spot urine (nitrate, pH, protein, glucose, ketones and blood) did not differ signficantly by occupational group.

Liver function tests results of all examinees were studied in detail. Outliers above the values for the study population on the following liver function tets were studied: YGT, SGPT, SGOT, bilirubin, LDH, and alkaline phosphatase (see computer printout of histrograms and related data in Figure 3). Five PBB workers had elevated levels but only one subject had an elevation on more than one test. Four electricians had elevated tests including two persons with more than one elevated test (Table XI).

Table XI lists for the individuals with elevated liver function tests other laboratory findings, medical histories, physical examination, and habits in order to explore a possible etiology of the abnormal tests. Of the five PBB workers, two admitted to moderate to heavy use of alcohol presently or in the past. Of the four steel workers, one was a heavy drinker, and two had serum hepatitis. Of the four electrical workers, one admitted moderate to heavy drinking and another was being treated for lymphoma.

Due to the small numbers and other possible explanations for the liver function tests, an occupational exposure accounting for these abnormalities cannot be postulated.

4. Endocrine

a. Thyroid function

The study documented four cases of hypothyroidism in 35 men* employed in the production of PBB/PBBO but none in the 89 control subjects.[36] The findings of an elevated TSH and low free thyroxine index indicate primary hypothyroidism; that is, disease of the thyroid gland rather than of the pituitary or hypothalmus.

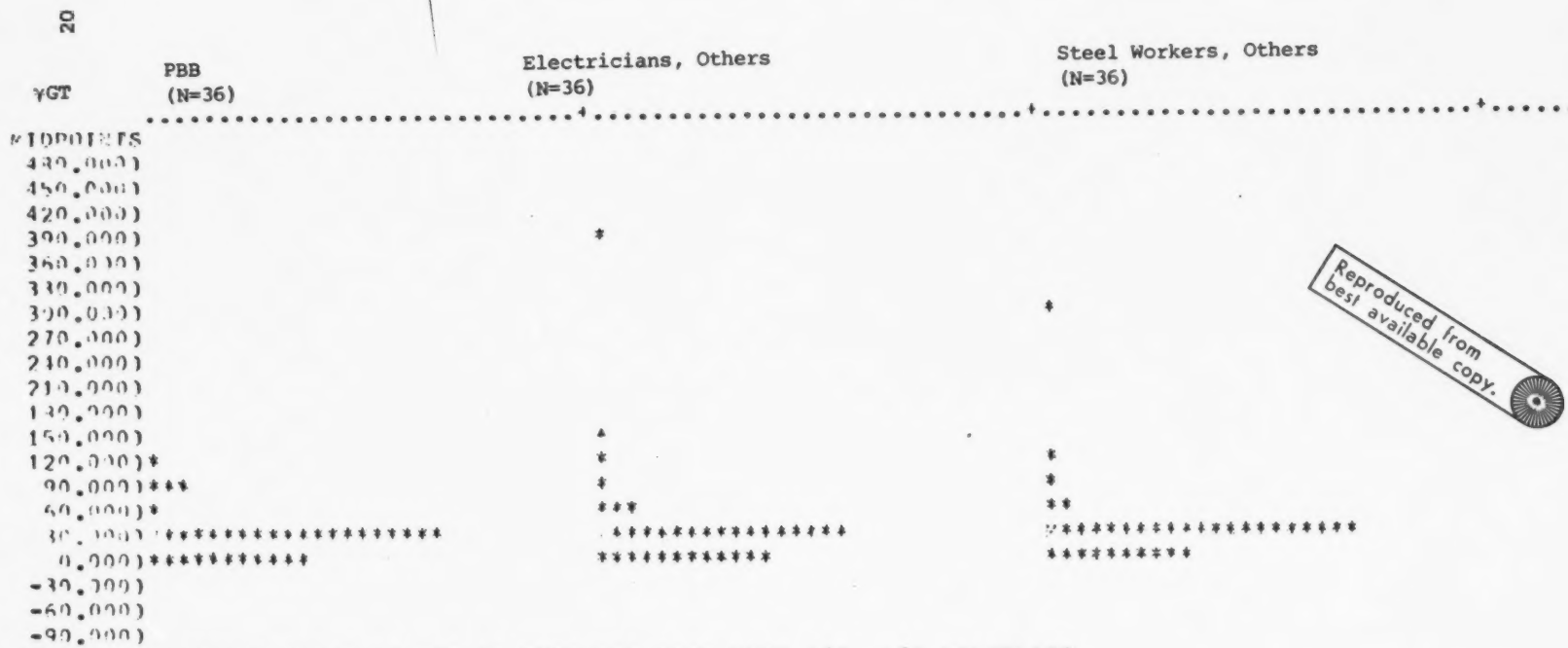
In the documented cases, the four men who had an elevated serum TSH had a low or borderline low serum T_4 and free thyroxine index. None of the 89 control subjects (including the 72 control (triad) subjects) had an elevated serum TSH. Since all subjects were questioned about occupational exposure to 74 toxic substances, it was determined that the three PBB and PBBO workers who had primary hypothyroidism had only three common exposures: PBBs, PBBOs, and bromine. The fourth worker who had hypothyroidism was known to have been exposed to PBBOs and bromine.

The PBB group had significantly more subjects with elevated serum concentrations of thyrotropin (P=0.006). The free thyroxine indexes (P=0.06) and serum T_4 concentrations (P=0.11) did not differ significantly. Although more PBB workers than controls had antimicrosomal antibody titers greater than 1:100, the difference between groups was not significant (P=0.06) (Appendix Table VII).

*Data were not available for one PBB worker due to a lost specimen.

FIGURE 3. Histograms of selected liver function tests for matched triads

γGT



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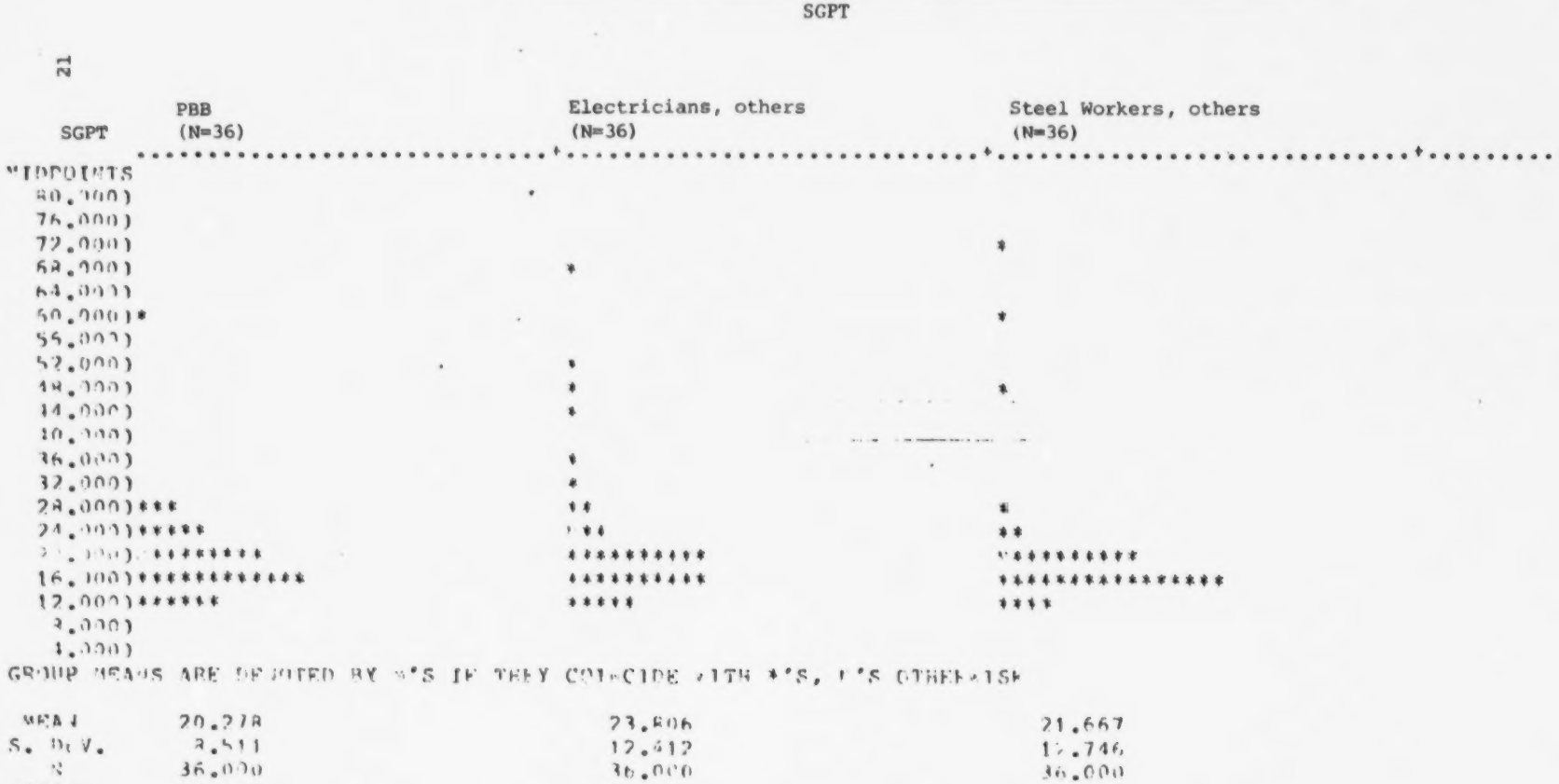
ALL GROUPS COMBINED (CASES EXCLUDED IF SPECIAL CODES FOR EITHER VARIABLE)

			SUM OF SQUARES	DF	MEAN SQUARE	F RATIO	PROB. F EXCEEDED
MEAN	36.741	BET.GRP	1362.9074	2	681.4537	0.2597	0.7718
S. DEV.	50.867	WITHIN	275191.8300	105	2623.7317		
N	108.	TOTAL	276554.7400	107			
MAXIMUM	382.000						
MINIMUM	7.000						

FIGURE 3. Histograms of selected liver function tests for matched triads (cont.)



GROUP MEANS ARE DENOTED BY *'S IF THEY COINCIDE WITH *'S, I'S OTHERWISE

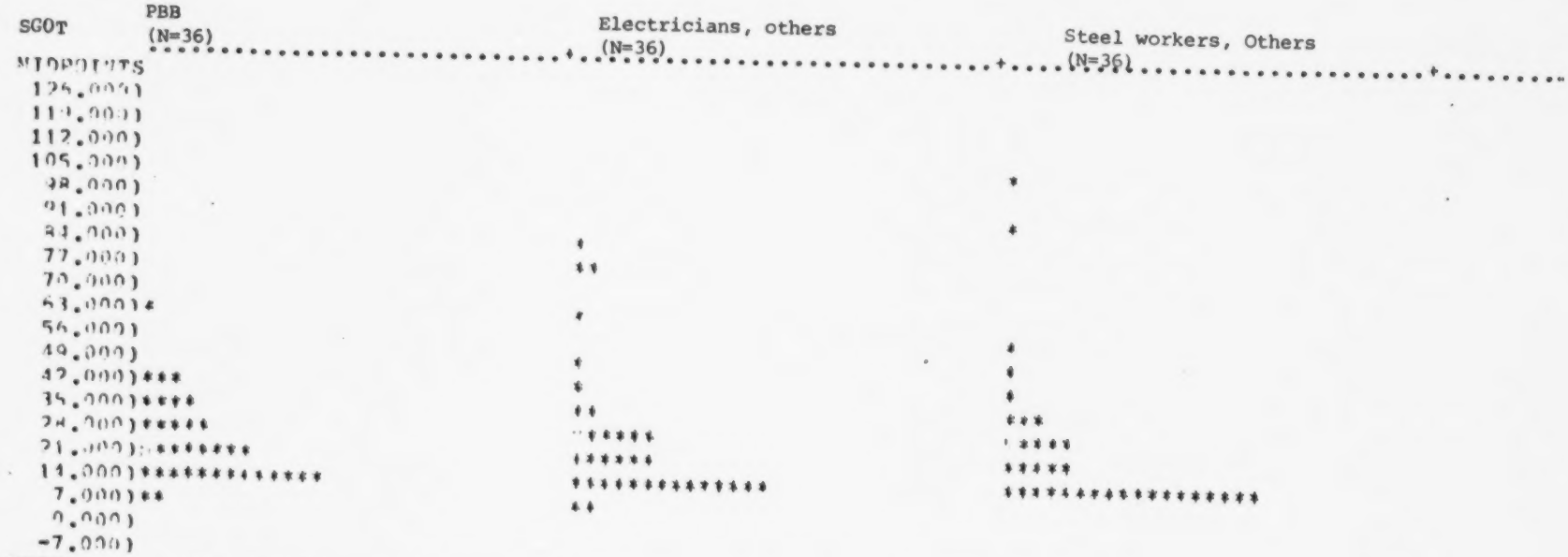
MEAN	20.278	23.806	21.667
S. DEV.	8.511	12.412	12.746
N	36.000	36.000	36.000
MAXIMUM	62.000	70.000	73.000
MINIMUM	12.000	12.000	13.000

ALL GROUPS COMPARED (CASES EXCLUDED IF SPECIAL CODES FOR EITHER VARIABLE)

			SUM OF SQUARES	DF	MEAN SQUARE	F RATIO	PROB. F EXCEEDED
MEAN	21.917	BETWEEN	227.3889	2	113.6944	0.8770	0.1191
S. DEV.	11.373	WITHIN	13612.8610	105	129.6463		
N	108.	TOTAL	13840.2500	107			
MAXIMUM	73.000						
MINIMUM	12.000						

FIGURE 3. Histograms of selected liver function tests for matched triads (cont.)

SGOT



GROUP MEANS ARE DENOTED BY A'S IF THEY COINCIDE WITH B'S, B'S OTHERWISE

MEAN	22.944	26.972	26.639
S. DEV.	11.357	10.481	20.942
N	36.000	36.000	36.000
MAXIMUM	60.000	87.000	107.000
MINIMUM	10.000	9.000	11.000

ALL GROUPS COMBINED (CASES EXCLUDED IF SPECIAL CODES FOR EITHER VARIABLE)

		SUM OF SQUARES	DF	MEAN SQUARE	F RATIO	PROB. F EXCEEDED
MEAN	25.519					
S. DEV.	17.695	BETWEEN	359.7063	2	179.8531	0.5699
N	108.	WITHIN	33143.1670	105	315.6492	
MAXIMUM	107.000	TOTAL	33502.8730	107		
MINIMUM	9.000					

FIGURE 3. Histograms of selected liver function tests for matched triads (cont)

TOTAL BILIRUBIN

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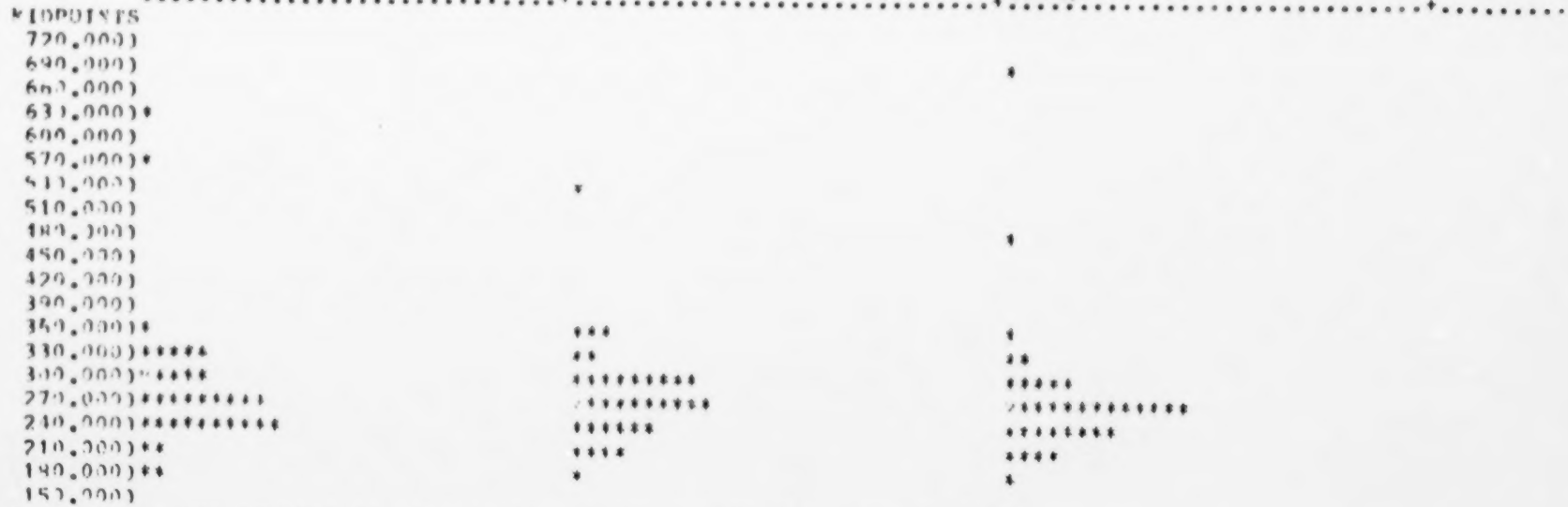
GROUP MEANS ARE DENOTED BY M'S IF THEY COINCIDE WITH #'S, #'S OTHERWISE

MEAN	0.466	0.338	0.391
S. DEV.	0.419	0.200	0.254
N	36.000	36.000	36.000
MAXIMUM	2.630	0.900	1.150
MINIMUM	0.100	0.030	0.060

ALL GROUPS COMBINED (CASES EXCLUDED IF SPECIAL CODES FOR EITHER VARIABLE)

			SUM OF SQUARES	DF	MEAN SQUARE	F RATIO	PROB. F EXCEEDS
MEAN	0.395	BETWEEN	0.3129	2	0.1565	1.6762	0.1920
S. DEV.	0.307	WITHIN	9.4015	101	0.0933		
N	106.	TOTAL	10.1144	103			
MAXIMUM	2.630						
MINIMUM	0.030						

FIGURE 3. Histograms of selected liver function tests for matched triads LDH (cont)



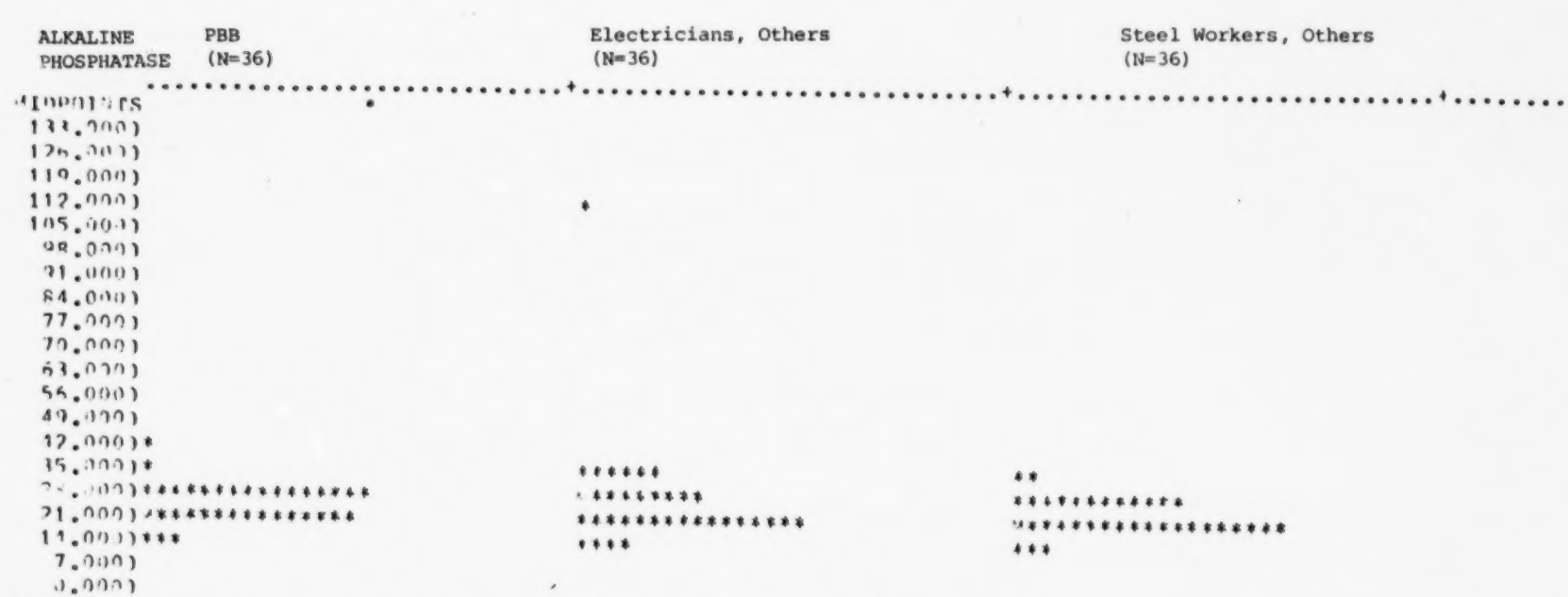
MEAN	285.750	283.222	282.139
S. DEV.	97.238	62.736	88.079
N	36.000	36.000	36.000
MAXIMUM	625.000	553.000	695.000
MINIMUM	187.000	193.000	189.000

ALL GROUPS COMBINED (CASES EXCLUDED IF SPECIAL CODES FOR EITHER VARIABLE)

			SUM OF SQUARES	DF	MEAN SQUARE	F RATIO	PROB. F EXCEEDED
MEAN	283.704	BETWEEN	247.2414	2	123.6207	0.0192	0.9810
S. DEV.	79.178	WITHIN	675643.2900	105	6434.6980		
N	108.	TOTAL	675890.5300	107			
MAXIMUM	695.000						
MINIMUM	187.000						

FIGURE 3. Histograms of selected liver function tests for matched triads (cont)

ALKALINE PHOSPHATASE



GROUP MEANS ARE DENOTED BY *'S IF THEY COINCIDE WITH #'S, +'S OTHERWISE

MEAN	24.083	27.194	24.194
S. DEV.	5.679	15.364	4.915
N	36.000	36.000	36.000
MAXIMUM	40.000	109.000	35.000
MINIMUM	15.000	13.000	14.000

ALL GROUPS COMBINED (CASES EXCLUDED IF SPECIAL CODES FOR EITHER VARIABLE)

			SUM OF SQUARES	DF	MEAN SQUARE	F RATIO	PROB. F EXCEEDED
MEAN	25.157	BETWEEN	224.2963	2	112.1481	1.1504	0.3205
S. DEV.	9.887	WITHIN	10236.0280	105	97.1560		
N	108.	TOTAL	10460.3240	107			
MAXIMUM	109.000						
MINIMUM	13.000						

One year after this study was performed, reevaluation of three of the four workers with hypothyroidism indicated 1) all three still had markedly elevated thyroid antimicrosomal antibody titers, 2) two still had low free thyroxine indexes and high thyrotropin values and 3) one had a normal free thyroxine index and a high-normal thyrotropin. None of these three workers had been treated with thyroid hormone.

PBBs, PBBOs and bromine must be considered as possible causes of the hypothyroidism in these workers because the plant produced only PBB and PBBOs and because PBBs or PBBOs and bromine were the only substances to which all four hypothyroid men were known to have been exposed. Animal studies describe a statistically significant decrease in serum T_4 concentration in rats after PBB administration.[37] This response was dependent on both time and dose. Serum concentration of thyrotropin in these animals was elevated. It is suggested that a defect in the iodination of tyrosine is a mechanism by which PBBs produce hypothyroidism in rats. Although studies of thyroid function have not been performed with PBBOs, thyroid hyperplasia has also been reported in rats given decabromobiphenyl oxide.

The subnormal serum concentration of T_4 five months after cessation of exposure in rats suggests a persistent effect of PBBs which could explain the hypothyroidism in two workers who had not been exposed to PBBs for five years before the study.

To our knowledge, there have been no other reports attributing human hypothyroidism to PBBs or PBBOs or elemental bromine; however, the development of thyroid abnormalities in animals given PBBs and PBBOs supports this hypothesis.

b. Reproductive function

Although a few subjects in the PBB study group had elevated LH's or FSH's, the differences among the three groups were not statistically significant. Testosterone levels of all PBB workers were within the normal range and no significant difference in mean values by worker group was found (Appendix Table VII). Futher investigation of these hormones is needed in relation to exposure.

4. Urine

Spot and 24-hour urines were analyzed for creatinine, porphyrins, glucaric acid, delta-aminolevulinic acid, and porphobilinogen. The spot urine values were analyzed as ratios to creatinine (see Table I). No significant differences were found in comparing the age-matched triads.

g. Nerve Conduction Tests

The following preliminary results serve the general purposes outlined above, namely for data cleanup and outlier detection, establishing the study's empirical distributions with means, s.d., ranges, etc., as well as allowing initial comparisons across a selection of groups.

A first comparison of all examinees (< 108) on whom nerve conduction measurements were made showed the following orderings for the means of the three groups (triads) comprising workers matched on race, sex and age, where P: PBB workers, S: Steel workers, and E: Electrical wiremen.

Triads (#2, Page 13)

Nerve Velocity	MMV	PMV	MSV*	USV*	SSV	LSSV
Order d Means	E<P<S	E<P<S	S<E<P	S<E<P	P<S<E	P<S<E
P-value	.1381	.0381	.6574	.8306	.0116	.0090

P values refer to (two-sided) F tests of the one-way ANOVA model.

Without exception, the cases with the lowest values for each nerve velocity were found to be examinees with known extraneous causes of neuropathy. As a result, although control for age by matching was lost thereby, 39 subjects were excluded (from futher analyses reported here) for the following reasons: 1 each with lymphoma, Charcot-Marie-Tooth atrophy (possible), carpal-tunnel syndrome and diabetes; 3 with both DM and excess alcohol intake (>4 drinks/day) and 32 with excess alcohol intake only. The following tables present analyses on groups comprised of 23 PBB (P), 31 electrical (E), 12 steel (S) and 16 other (O) white male workers from the area. Of these there are three missing median motor, two missing peroneal motor, and one missing sural sensory values due to factors at the time of the examination, e.g., patients requesting that the testing be stopped. Numbers in brackets refer to group sizes in the analysis following these exclusions.

The next table reports one-way ANOVAs excluding all subjects with known extraneous cause for neuropathy. Results of one-way ANOVAs across the four groups and across the three groups defined by industrial occupations were:

Four Groups (#3', Page 14)

Nerve Velocity	MMV[72]	PMV[72]	SSV[72]	LSSV[72]
Order Means	E<P<O<S	E<P<O<S	P<O<S<E	P<O<S<E
P-Values	.1549	.1341	.0979	.0910

*MSV and USV will not be reported further here as they did not show the capability to discriminate between occupation groups in these univariate analyses.

Three Groups (#3', excluding "others")

Nerve Velocity	MMV[62]	PMV[62]	SSV[62]	LSSV[62]
Ordered Means	E<P<S	E<P<S	P<S<E	F<S<E
P-Values	.0627	.0544	.1038	.0858

The F statistic in a test for differences in age across these three groups showed a P-Value of .0423 with mean ages ordered as S[32.92]<P[33.95]<E[41.54]. With the exception of sural sensories, all nerve velocities were negatively associated with age for the study as a whole. However, correlation coefficients of nerve velocities within occupational groups suggested varying degrees of linear association with age. In particular, it is noted below that the PBB workers differed almost significantly from the controls in the degree of linear association of MMVs on age.

An analysis of variance across three groups with age entered as a covariate gave the following results. Here, P values refer to the F test for zero slope in the analysis of covariance. P' measures the probability that the slopes (in the linear regressions of nerve conduction velocities on age) within groups are equal.

Three Groups with Age as Covariate (#3', Page 14, excluding "others")

Nerve Velocity	MMV[62]	PMV[62]	SSV[62]	LSSV[62]
P-Values	.0242	.0495	.4190**	.4371**
P'-Values	.0616***	.3825	.4960	.4769

The slopes of the sample linear regressions of MMV on age within groups were ordered as S(-.2664)<P(-.2121)<E(-.0072). The validity of the analysis of covariance model for age adjustment within PBB and steel workers only was established (P' = .7286, P = .0040).

Pending further investigations in regard to the normality and homoscedasticity assumptions on these responses, as well as a much more detailed look at the question of whether a linear, as contrasted with other functional associations, were the correct model for the relationship between the nerve conduction velocities and age, the following results were observed as suggesting a measure of neurotoxicity among the PBB workers. P* refer to one-sided t-tests of the indicated pairwise contrasts of group means (adjusted if so stated). We include a statistically valid ANCOVA across two groups, in which MMVs of PBB workers approach, but do not achieve, an .05 level of significance.

**Analyses of covariance not appropriate; surals were not linearly associated with age.

***The special assumptions required for an analysis of covariance model are barely met; hypothesis of equality of slopes within groups must be questioned. The F statistic testing the assumption of a parallel dependence of median motor velocities on age within PBB and control groups approached significance, with P = .0616. Although the one-sided t-test for the contrast of PBB workers with the steel workers is reported tentatively as significant, a thorough investigation with careful choice of adjustment for the age differences found here is indicated.

Three Groups Comparison on SSV, PMV and MMV

ANOVA	Nerve Velocity	SSV[62]	LSSV[62]
	P-Values	.1038	.0858
	Ordered Means (Unadjusted)	P<S<E	P<S<E
		P* < .025 (t = 2.1648)	P* < .025 (t = 2.2571)
ANCOVA	Nerve Velocity	PMV[62]	MMV[62]
	P-Value	.0495	.0242
	Ordered Adjusted Means	P<E<S	P<E<S
		P* < .05 (t = 1.9655)	P* < .05 (t = 1.7853)

Two Groups Comparison on MMV

ANCOVA	Nerve Velocity	MMV[34]
	P-Value	.004
	Ordered Adjusted Means	P<S
		.05 < P* < .10 (t = 1.6244)

Communications with the neurologist supervising the electromyographic studies had suggested that age was acting as a surrogate variable here, as nerve velocities are not known to decrease with age in normal populations. It was suggested that information collected at the field study on exposures to lead, as a heavy metal, and to carbon tetrachloride, a solvent, should be investigated as possible explanatory variables for the decline in the four velocities indicated. Of course, the most important class of variables to be investigated next would measure extent of exposure to PBB, e.g., serum PBB levels.[1)]

PBB, PBBO, AND PCB SERUM LEVELS

The plasma sample analysis for polychlorinated biphenyls (PCBs), polybrominated biphenyls (PBBs), and polybrominated biphenyl oxides (PBBOs) was performed at the Research Triangle Institute (RTI), North Carolina.

Standard methods used by Research Triangle Institute for the extraction and cleanup of PCBs and PBBs were followed with one modification. The sample and solvent volumes were reduced by half. This change was necessitated by the fact that only 4 to 5 ml. of serum was received rather than 10 m. as requested by the laboratory. The extraction and the cleanup procedure is given in detail in the laboratory report submitted by RTI to the American Public Health Association, No. RTI/1747/00-F, dated October 25, 1979.

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1) The results of the laboratory procedures were not available in time to be included in the preliminary analyses reported here. Further analyses of the associations of peroneal motor, median motor, and median sensory nerve conduction velocities using a multiple linear regression model, with age, lead and carbon tetrachloride, three measures of length of employment at the plant and PBB serum levels as explanatory variables are to appear shortly.

The extraction and cleanup procedure was validated using gas chromatography/electron capture gc/ecd as recommended by the Standard Procedures. Serum samples were spiked at 58 ng/ml with hexabromobiphenyl. Two extracts gave 76 and 75 percent recovery for the entire population.

In order to obtain positive identification as well as quantitation, the technique of gas chromatography/masspectrometry/computer (GC/MS/COMP) was used for the analysis of the serum extracts. This technique has been used to identify and quantitate PCBs, PBBs as well as PBBOs in a variety of samples including the identification of PBBO in human hair. Limits of detection for the reduced sample size ranged from below 1 ng/ml to 25 ng/ml. depending upon the molecular weight and gas chromatographic retention times. The details of the GC/MS/COMP and all the laboratory results (using new identification numbers in random order) are given in the above RTI report.

The distribution of the total serum levels of PBBs, PBBOs, and PCBs, among the occupational groups (PBB workers, electricians, steel workers, and others) is described in Appendix Table XII. The number of cases with detectable levels of each of the chemicals analyzed, as well as the minimum and maximum levels, are shown in Appendix Table XIII.

As indicated in Appendix Table XII, a significantly higher number of PBB workers had a detectable level of PBBs as compared with other workers in the study (35.9 percent as compared to 12.1 percent, chi-square = 8.67, $p<0.005$). Among workers with detectable PBB levels, the PBB workers had significantly higher serum levels ($p<0.001$) as compared to other workers ($Z = 3.61$, Mann-Whitney U test). No significant difference in the frequency of detectable levels of PBBOs and PCBs nor in the absolute values of these chemicals was found among the occupational groups.

It should be noted that although the factory concentrated on manufacturing decabromobiphenyl and decabromobiphenyl ether, there was no positive identification of $C_{12}Br_{10}$ or $C_{12}Br_{10}O$. This finding should be explained by the facts that not all the studied chemicals have similar persistence and that the hexabromobiphenyl may be more persistent than the decabromobiphenyl. Also, the decabromobiphenyl ether would be more easily metabolized and excreted. As Dr. Renate D. Kimbrough indicated in a letter dated May 30, 1978, "Analysis for decabromobiphenyl ether may be difficult. The decabromobiphenyl is probably not absorbed as efficiently by mammals as hexabromobiphenyl." Apparently only $C_{12}H_9BrO$ and $C_{12}H_7Br_3O$ were detected, and in relatively low dosages.

These findings imply that any study of health effects related to PBBO exposure should be based on employment characteristics (such as period of employment, job description, etc.) rather than on PBBO serum levels alone. Accordingly, adverse health effects related to industrial PBB exposure should be discussed in view of both employment data and serum levels.

h. Female Subjects

Eight females, aged 21 to 47 years, were studied including 3 PBB females and 5 control subjects. No separate sex-specific analyses were performed due to the small number of subjects. However, the medical, reproductive and social histories, general physical examinations, and laboratory results were reviewed in detail. Only one woman, a steel worker, had a significant medical condition, chronic hepatitis with elevated liver function tests (Table XI). Two women had had hysterectomies and one was menopausal, explaining their elevated levels for LH and/or FSH. Two women had had several miscarriages; neither one was a member of the PBB group.

LIMITATIONS AND SUGGESTED FURTHER ANALYSIS

1. Comparative Analysis

This was an initial, exploratory search for possible adverse health effects in human subjects occupationally exposed to PBBs. Only univariate distributions have been examined and preliminary analyses necessarily were concerned with comparisons across study and control groups on univariate responses. Since the 36 cases in each triad were age-matched, all analysis of variance tests across the three study triads that have been reported here (with the exception of the nerve conduction studies as noted) have controlled for age. Thus, further studies can be undertaken within a quasi-experimental design in which age-matched group sample sizes could be projected to confirm, at a preassigned power, the existence of suggested effects estimated from this study.

However, it is inherent in the observational character of an occupational health effect study that biases due to extraneous, possibly confounding, factors (i.e., those not "randomized out") be controlled for via the appropriate post hoc analysis. For a large number of the responses in this investigation, a larger than expected, or "normal", range was observed. The alternative hypothesis which postulated that this variation was due simply to occupational exposure to PBBs could not be established for almost all of these responses. Comparisons across study and control populations would be more discerning if control of extraneous variation due to factors associated with the response whose distributions differ across treatment groups, were attempted.

Further, various multivariate procedures could be pursued for the numerous laboratory responses which exhibited a wider than expected spread. An initial inquiry into possible correlated factors has suggested variables which should be investigated via multivariate methodologies, e.g., lead exposures correlated significantly with several nerve conduction velocities. Explanatory correlates could be investigated as competing factors, for example, in multiple regression models,if linear associations are either present or can be effected. The latter will require careful exploratory procedures to detect the appropriate transformation.

It is possible that a linear combination of several responses would be more effective in discriminating among groups than any single variate investigated here. Statistical stepwise procedures for selecting "best" subsets from variables which show some difference across groups in these tables would suggest appropriate vectors of variates.

In conclusion, although the univariate analysis employed here exhibited limited capability to distinguish occupational groups for most responses, the next step is to select combinations of responses which may prove to be more effective. Significant correlations (between the laboratory variables themselves as well as between variables and concomitant factors such as exposure to other possibly toxic agents) should be investigated. More detailed statistical models would utilize the exhibited associations to explain the more than normal variation that has been found in numerous responses in these preliminary analyses.

2. Analyses Specific to PBB Exposure

The primary objective of the study was to determine the adverse health effects related to PBB occupational exposure, as compared to other neighborhood industrial workers. A valid and meaningful analysis should be from a "dose-response" approach. However, in the absence of the PBB, PBBO, and PCB serum levels, only general employment characteristics such as period and length of employment were taken into consideration. Moreover, the univariate approach to the analysis of the data considered the place of employment only as a stratum, i.e., the exposure characteristics were limited to whether a person had ever been or had not been exposed to PBB/PBBO, regardless of the level of exposure. This approach was very limited as it completely ignored any indication of the level of exposure. The PBBs are highly lipotropic substances which are not easily metabolized or biodegraded; therefore, the current serum level can represent the accumulated detectable exposure. Assessment of the accumulated exposure, together with employment characteristics and manufacturing data may lead to identifying high risk exposure periods. In addition, in the analyses of health effects-related exposure, one should look not only for the people with adverse health effects, but for trends and the association between biological variates and level of exposures within a given "normal range". Based on the observed serum levels, we believe that the preliminary analysis was unable to identify more adverse health effects if they existed because of the heterogeneity of the PBB workers with respect to dose and duration. Therefore, we suggest that the serum level of PBB/PBBO be examined as a function of employment variables. We will then be able to identify a subgroup of workers with a significant high level of exposure. The records of these people should be examined to determine whether they have an excess of adverse health effects.

In addition to the simple dichotomy examined in the current study (i.e., PBB/not PBB employment), in order to complete the statistical analysis it will be necessary to:

1) define an index which describes a gradient of exposure to PBB. This index of exposure would be based on a choice from the following multiple parameters:

a) PBB serum levels
b) period of "active" exposure to PBB (i.e., length of employment at the plant during period of actual PBB production)
c) duration of "passive" exposure (i.e., length of time since last exposure).

2) examine the statistical association between the above index and the medical variates. An unfavorable trend, even within the "normal" range of the laboratory tests, may indicate more health problems in the future.

3. Epidemiological Considerations

The determination of whether occupational exposure to toxic substances such as PBBs and PBBOs produced adverse health effects necessitates a carefully planned analysis of the subsequent mortality or morbidity experience over time of a group exposed to the factor under consideration. In interpreting differences in morbidity and mortality among occupational groups, it must be remembered that 1) state of health itself may determine entry into a specific occupation and 2) the current co-worker group will not include those who have left employment due to the deleterious occupational exposure although using the cohort approach may have minimized some of these deficiencies.

An important limitation of the present study was the inadequate follow-up time subsequent to PBB exposure. A longer period of observation could result in identification of adverse health effects which would not be apparent in a shorter time span. A similar study at a later date may detect latent adverse health effects associated with PBB exposure.

SUMMARY

During the last week of August, 1978, a study of 36 men who had been exposed to PBBs and PBBOs in their working environment for at least six weeks between January, 1973 and August, 1978, was carried out. The plant had manufactured PBB and PBBO until production of the former was terminated in April, 1977. Following cessation of the manufacture of decabromobyphenyl, the factory concentrated on producing decabromobyphenyl ether.

Controls were selected from workers employed in the same community without exposure to PBB and PBBO with an attempt to match the exposed population by age and race.

In addition to demographic, smoking, drinking and lifetime occupation questionnaires, self-reported medical histories, on-site general physical and dermatological examinations, neurological and nerve conduction studies and laboratory tests of urine, blood, including PBB serum levels, and measures of liver, thyroid and reproductive functions, were performed.

Analysis of the data focused on:

1) Description of the univariate distributions of the laboratory variates. Study ranges (95 percent) are reported in addition to analogous "normal" intervals found in the literature.

2) Comparison of the distributions of the variables across various selections of occupational groups, in particular the age, sex and race matched triads, using the analysis of variance F-test for interval-scale measurement and chi-square tests for classifications. For the nerve conduction velocities, adjustment for age was made with an analysis of covariance model, where assumptions were met.

Conclusions are:

1) As can be read in Table II, for the study as a whole, a large majority of responses show either a wider than normal 95 percent range and/or a distribution that is off-center, frequently in a direction implying health impairment. For example, all five nerve velocities studied are reduced, suggestive of neurotoxicity for the study as a whole.

2) As can be seen from Table V to IX, procedures which were used to test for differences across occupational groups (the triads) very rarely showed significance. The several medically-isolated instances, e.g., serum phosphorus ($P = .03$, Table VII), may well be chance associations.

However, for two categories of variates, an adverse health effect from occupational PBB exposure may be postulated. As reported on Page 19, this study found a significantly increased incidence of hypothyroidism among the PBB workers.[36] Also, sural sensory velocities (discussed on Page 28) have shown a significant reduction ($P < .025$) when compared with the electrical wiremen. Following adjustment for age, peroneal motor velocities are reduced ($P < .05$) when compared with the steel group. Pending further adjustment procedures for age, it is possible that the PBB median motor velocities also are reduced. Further investigations in regard to both hypothyroidism and nerve velocities, in particular, looking for possible dose-response associations within the PBB group, are warranted.

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TABLE I

Hematologic, Serologic, Urinary and Electrodiagnostic Tests, Methods of Collection, and Testing Laboratory

BLOOD (NON-FASTING SPECIMEN) LABORATORY TESTS*

I. TEST	METHOD OF COLLECTION	TESTING LABORATORY
A. CBC, Differential, hemoglobin and and hematocrit SMA 24 (glucose, BUN, creatinine, Na, Cl, K, CO_2 as bicarbonate, uric acid, Ca, P, total protein, albumin, globulin (total), alkaline phosphatase, bilirubin indirect and direct, cholesterol, SGOT, SGPT, LDH, triglycerides, ratio BUN/creatinine, ratio albumin/globulin) plus YGT. Resin T_3 Uptake	(1) 7 ml. purple top (EDTA) tubes must be examined within 24 hrs. (3) 10 ml. red top tubes (Corvac) Allow to stand at room temperature for 30-60 minutes for clot retraction. Then centrifuge at 6000 RPM for 10-15 minutes. Refrigerate immediately.	Dr. Leslie M. Shaw, Director Toxicology Laboratory, Division of Laboratory Medicine, Pathology Department, HUP Bioscience Laboratories
B. Testosterone assay FSH, LH, and TSH assay, T_4 Triiodothyronine T_3 (if hyperthyroidism suggested by T_4 and TSH values), thyroid antibodies (if hypothyroidism indicated by T_4 and TSH) All of above by radioimmunoassay except thyroid antibodies	(2) 10 ml. red top tubes (Corvac) Handle as above Freeze within 12 hours	Dr. Peter Snyder, Endocrine Section, Dept. of Medicine, U of P School of Medicine Remaining serum kept frozen indefinitely Bioscience Laboratories
C. PBB, PBBO, PCB levels in serum	(2) 10 ml. red top (Corvac) Obtain serum from whole blood as above. Aspirate serum into glass scintillation vial and refrigerate immediately. Freeze within 12 hrs.	Research Triangle Institute - North Carolina Dr. Etio Pellizzari

*10% of all samples retested.
All specimens were brought back to the respective laboratories in Philadelphia at the end of each day by courier from Bioscience Laboratories.

TABLE I (continued)

URINE LABORATORY TESTS*

II. TEST	SPECIFICATIONS	RESPONSIBILITY FOR LAB WORK
A. Ratio of the following parameters to creatinine. 1. porphobilinogen 2. delta-aminolevulinic acid 3. coproporphyrins } total 4. uroporphyrins } porphyrins Creatinine mg/ml	Pour urine into Bioscience plastic vial A1 for assay of 1, 2, and 3, vial A8 for assay of 3 and 4. Refrigerate immediately. Freeze A1 within 12 hours. Protect from light.	Dr. Carl Alper, Bioscience Laboratories
B. Ratio glucaric acid to creatinine.	Pour urine into container provided by U of P laboratory. Refrigerate immediately.	Dr. Leslie M. Shaw, Pepper Lab, HUP

The urine tests were done on both a spot sample and a 24-hour sample when available. To standardize the collection of spot urines, screenees were asked to void 2 hours before entry. Upon entry, and over the 3 hour period at the exam site, the screenee collected his urine in a 500 cc. flask. Only sugar-free soda and water were offered to screenees until all samples were collected.

The 24 hour urines were collected in ½ gallon jugs (Bioscience Lab) wrapped in paper bags. Preservatives or refrigeration were not required.

Total volume of both spot and 24-hour urines were measured and then aliquots from each handled identically as indicated above.

QUALITATIVE URINE TESTS

Dr. Shaw's research assistant did qualitative urine dipstick on each specimen on site at the laboratory to determine pH, glucose, blood, protein, ketone, nitrites.

ELECTRODIAGNOSIS

TABLE I (continued)

III. TEST	METHODS	RESPONSIBILITY FOR LAB WORK
A. Sensory nerve conduction arm: median ulnar leg: sural TECA Electromyogram & Averager	1) stimulate nerve distally by ring electrodes on fingers and surface on foot. 2) proximal recording (NAP) by surface electrodes at one or more points; orthodromic	Prof. R.E. Lovelace, Director of EMG & Clinical Neurophysiology Laboratory, Neurological Institute, NY, 710 W. 168th St., NY, NY 10032 (& colleagues including Ms. Betty Hughley).
B. Motor nerve conduction arm: median leg: peroneal TECA Electromyogram & Averager	1) stimulate nerve at one or more proximal points and one distal. 2) record distal MAP orthodromically by surface electrode over motor point.	
C. F-Waves leg: peroneal TECA Electromyogram & Averager	"Rebound" late response on supramaximal motor stimulation as above (compute from L1/T12). In A, B & C above exact temperature recording control and monit oring essential.	

TABLE II

Normal Range and Study Results of Test Variables

	Normal Range	STUDY RESULTS		
		Mean	Std. Dev.	95% of Study
A. Nerve conduction				
1. Median motor	>50.3	57.291	5.129	>50.0
2. Peroneal motor	>45.6	46.206	4.399	>39.8
3. Median sensory	>50.9	54.366	6.371	>44.8
4. Ulnar sensory	>42.7	50.585	5.842	>41.1
5. Sural sensory*	>40.3	46.750	6.047	>37.1
B. Hematology				
1. Hemoglobin (gms %)	M 14-18 F 12-16	15.388	1.037	M 13.7-17.5 F† 13.3-15.2
2. Hematocrit (%)	M 38-54 F 36-47	43.630	3.090	M 38.5-49 F† 37.5-44
3. Red blood cells (RBC) (millions/mm^3)	M 4.5-6.0 F 4.3-5.5	4.896	0.412	M 4.1-5.5 F† 4.1-5.0
4. Mean Corpuscular Vol. (MCV) (micron^3)	79-99	89.159	5.019	81-97
5. Mean Corpuscular Hemglobin (MCH) γ/γ	27-35	31.558	1.929	28.5-34.5
6. Mean Corpuscular Hemoglobin Concentration MCHC (%)	22-37	35.202	0.968	33.9-36.6
7. Leucocytes (1000/mm^3)	5-10	7.463	1.960	4.5-11.5
8. Neutrophils (%)	40-60	53.195	9.935	37-71
9. Band (%)	0-5	4.775	3.477	0.5-12.5
10. Eosinophil* (%)	1-3	2.036	1.757	0.2-5.5
11. Basophil* (%)	0-1	0.493	0.776	0-2.9
12. Monocyte (%)	4-8	6.674	3.344	1.5-13.5
13. Lymphocyte (%)	20-40	32.905	8.845	16.5-49.5

* A logarithmic transformation was made for these variables (see Page 13)
† For 8 females -- 100% range of the study

TABLE II (continued)

Normal Range and Study Results of Test Variables

	Normal Range	STUDY RESULTS		
		Mean	Std. Dev.	95% of Study
C. Blood Chemistry				
1. Sodium (meq/L)	138-146	141.094	2.746	136-145
2. Potassium (meq/L)	3.5-5.3	4.195	0.357	3.7-5.0
3. Chloride (meq/L)	97-108	102.401	3.083	96-106
4. Carbon dioxide (CO_2) (mM/L)	24-32	24.043	1.981	21-27
5. Blood urea nitrogen (BUN) (mg/dl)	10-20	15.664	4 138	8-25
6. Creatinine (mg/dl)	M 0.8-1.4 F 0.7-1.2	1.115	0.163	M 0.9-1.4 F† 1.0-1.0
7. Glucose* (mg/dl)	60-105	85.875	22.556	68-113
8. Calcium (mg/dl)	8.5-10.5	10.027	0.430	9.4-10.9
9. Phosphorus (mg/dl)	2.4-4.4	3.488	0.597	2.3-4.7
10. Total protein (g/dl)	5.8-7.4	7.871	0.442	6.9-8.6
11. Uric acid (mg/dl)	M 3.5-8.0 F 3.0-6.0	5.648	1.388	M 4.5-8.5 F† 2.9-4.6
12. Acid phosphatase (U/L @ 30° C)	1.7-5.0	2.717	0.533	1.5-3.5
13. Cholesterol (mg/dl)	see note following #23	190.416	31.744	135-255
14. Total bilirubin (mg/dl)	0.2-1.2	0.425	0.483	0.1-1.1

TABLE II (continued)

Normal Range and Study Results of Test Variables

	Normal Range	STUDY RESULTS Mean	Std. Dev.	95% of Study
C. Blood Chemistry (continued)				
15. Aspartate Amino Transferase* (SGPT (U/L @ 30°C)	M 9-38 F 6-25	23.625	16.495	M 11-81 F† 10.5-477
16. Gamma Glutamyl Transferase* (γGT) (U/L @ 30°C)	M 6-40 F 4-24	33.153	46.735	M 5-130 F† 9-67
17. Lactic acid dehydrogenose (LDH) (U/L @ 30°C)	140-270	281.116	77.174	195-555
18. Albumin (g/dl)	3.6-4.8	5.031	0.334	4.4-5.6
19. Globulin (g/dl)	1.6-3.5	2.838	0.354	2.3-3.6
20. Albumin globulin ratio	1.1-2.2	1.812	0.273	1.4-2.3
21. Alanine Amino Transferase* (SGOT) (U/L @ 30°C)	M 10-25 F 9-22	23.625	16.495	M 10-81 F† 9-15
22. Alkaline phosphatase (U/L)	12-40	24.941	9.211	16-39
23. Triglyceride* (mm ol/L)	see note following #23	1.993	1.592	1.02-6.75[1]

Note

	CHOLESTEROL[2] Normal Ranges		TRIGLYCERIDES[2] Normal Ranges
0-19 years	<190 mg/dl	<1.58 mmol/L	(140 mg/dl)
20-29 years	<220 mg/dl	<1.58 mmol/L	(140 mg/dl)
30-39 years	<240 mg/dl	<1.70 mmol/L	(150 mg/dl)
40-49 years	<270 mg/dl	<1.81 mmol/L	(160 mg/dl)
50-59 years	<290 mg/dl	<2.15 mmol/L	(190 mg/dl)

[1] High levels in some individuals probably due to recent meal
[2] Constant diet and 12-16 hour fasting necessary prior to sampling

TABLE II (continued)

Normal Range and Study Results of Test Variables

	Normal Range	STUDY RESULTS		
		Mean	Std. Dev.	95% of Study
D. Endocrine				
1. Testosterone (mg/dl)	300-1200	648.182	225.062	330-1050
2. Follicle Stimulating Hormone* (FSH) (mIU/ml)	<14	8.466	14.596	1.2-15
3. Luteinizing Hormone* (LH) (mIU/ml)	<18	11.723	15.186	1.6 (99%)
4. Thyroxine (T_4) (µg/dl)	4.5-11.5	10.283	13.604	7.0 (99%)
5. Thyroid Stimulating Hormone* (TSH) (µU/ml)	<8	5.161	15.521	7.7 (99%)
6. Resin Uptake Ratio (RUR)	0.85-1.17	1.005	0.776	1.0 (99%)
7. Free Thyroxine Index (FTI)	3.8-10.8	10.349	15.663	7.02 (99%)
E. Urine Spot:				
1. Creatinine (mg/l)		969.335	676.088	275-2850
2. Delta-Aminolevulinic Acid (mg/l/mg creat.)		2.136	1.320	1.2-5.5
3. Porphobilinogen quant. (M/l/mg creat.)		0.751	0.583	0.19-2.03
4. Corphoporphyrin (M/l/mg creat.)		89.153	61.800	34-210
5. Uroporphyrin (M/l/mg creat.)		9.978	9.848	1.0-28
6. Gluaric acid (U moles/l/mg creat.)				10-43

TABLE II (continued)

Normal Range and Study Results of Test Variables

	Normal Range	STUDY RESULTS		
		Mean	Std. Dev.	95% of Study
F. Urine (continued)				
24-Hour Urine:				
7. Creatinine (mg/24 hr)	1000-16000	1134.525	562.416	375-2475
8. Delta-aminolevulnic acid (mg/24 hr)	1.3-7.0	2.615	1.209	0.90-5.4
9. Porphobilinogen (ug/24 hr)	0-2.8	0.681	0.447	0.08-2.0
10. Corphoporhyrin (ug/24 hr)	50-250	81.632	60.843	15-165
11. Uroporphyrin (ug/24 hr)	10-50	13.040	8.004	4.5-31.5
12. Glucaric acid (m moles/24 hr)	4-74			10-35

TABLE III

THE 36 STUDY TRIADS (MALES ONLY)

Triad Number	PBB Workers		Electricians & Others			Steel Workers & Others		
	Number	Birth Year	Number	Birth Year	Age Diff.[1]	Number	Birth Year	Age Diff.[1]
1	002	1956	007[2]	1956	0	005	1956	0
2	009	1955	006[2]	1956	+1	004	1956	+1
3	008	1955	018[2]	1954	-1	003	1956	+1
4	012	1954	017[2]	1954	0	011	1955	+1
5	025	1953	016[2]	1954	+1	015	1954	+1
6	024	1953	027[2]	1953	0	014	1954	+1
7	023	1953	034[2]	1952	-1	013	1954	+1
8	022	1953	043[2]	1951	-2	026	1953	0
9	021	1953	029	1952	-1	032	1952	-1
10	020	1953	030	1952	-1	031	1952	-1
11	028	1952	039	1951	-1	040	1951	-1
12	036	1951	038	1951	0	041	1951	0
13	044	1950	037	1951	+1	046[2]	1950	0
14	047	1949	045	1950	+1	050	1949	0
15	054	1948	049	1949	+1	059	1948	0
16	053	1948	056	1948	0	058	1948	0
17	052	1948	055	1948	0	057	1948	0
18	051	1948	062	1947	-1	063[2]	1947	-1
19	060	1947	061	1947	0	066[2]	1946	-1
20	071	1944	067	1945	+1	070	1945	+1
21	083	1938	075	1940	+2	074	1941	+3
22	084[3]	1938	073	1942	+4	082[3]	1939	+1
23	089	1937	081	1939	+2	078[2]	1940	+3
24	088	1937	080	1939	+2	077[2]	1940	+3
25	087	1937	085	1938	+1	076[2]	1940	+3
26	092	1936	093	1936	0	086[2]	1938	+2
27	091	1936	097	1935	-1	090[2]	1937	+1
28	095	1935	101	1931	-4	102	1931	-4
29	094	1935	100	1931	-4	108	1930	-5
30	111	1928	113	1928	0	106	1930	+2
31	112[3]	1928	114	1928	0	109[3]	1930	+2
32	119	1925	122	1924	-1	110	1929	+4
33	125	1923	121	1924	+1	116[2]	1928	+5
34	124	1923	127	1923	0	131[2]	1921	-2
35	123	1923	126	1923	0	133[2]	1920	-3
36	129	1921	130	1921	0	135	1918	-3
Mean		42.3		42.3			42.7	
S.D.		11.15		11.18			11.22	

Note: I.D. number recoded for matching purposes.

[1] Age Diff. is age difference in years between the PBB worker and his matched case.

[2] Subject from residual control category.

[3] Member of a minority race.

TABLE IV

Preliminary Statistical Analysis of Laboratory Tests*

a. ANOVA among tested groups

Variable analysis \ Grouping	1 total	Test for normality	2 (triads)	3 (employment)	3'	4 (PBB vs. controls)	4' workers	5 (10 groups)
Urine	X	-	X	-	-	-	-	X
Endocrine	X	X	X	X	-	X	-	X
Hematology	X	X	X	-	-	-	-	X
Blood Chemistry	X	X	X	-	X	-	-	X
Nerve Conduction	X	X	X	X	X	-	X	X

b. Analysis of covariance (age)

Nerve Conduction	-	-	-	-	X	-	X	-

c. Correlation of laboratory data with age

	On original variables	On transformed variables
Urine	-	-
Endocrine	X	X
Hematology	X	X
Blood Chemistry	-	-
Nerve Conduction	X	X
Nerve Conduction (medical exclusions)	X	X

d. Correlation of laboratory data with length of employment at PBB production plant

Urine	-	-
Endocrine	X	X
Hematology	X	-
Blood Chemistry	X	-

X indicates analyses was performed
- indicates analyses not considered appropriate or necessary

*Utilizing BMDP Biomedical Computer Programs (Dixon, 1977)

TABLE V

Reported Symptoms by Occupational Group

System	PBB Workers (n=39) Number of persons	%	Electricians (n=42) Number of persons	%	Steel Workers (n=26) Number of persons	%
General, e.g., weight loss fatigue	15	38.5	13	31.0	9	34.6
Eyes, ears nose, throat	14	35.9	17	40.5	12	46.2
Respiratory	13	33.3	15	35.7	10	38.5
Gastrointestinal	10	25.6	9	21.4	10	38.5
Genitourinary	12	30.8	17	40.5	8	30.1
Endocrine	19	48.7	19	45.2	12	46.2
Dermatologic	27	69.2	32	76.2	17	65.4
Musculoskeletal	12	30.8	17	40.5	8	30.1
Neurologic	22	56.4	26	61.9	14	53.4

No significant difference was found between the three study groups (Chi-square test).

TABLE VI

Number of Workers with Abnormal Neurological Findings

Group / Neurologic aspect	PBB (39)	Electricians (42)	Steel Workers (26)	Others (28)
Cranial nerves	9	6	5	3
Pathological reflex	2	1	-	4
Deep tendon reflex	2	7	6	2
Motor and coordination	-	-	-	-
Gait and stance	-	-	-	1
Tremor	4	3	3	1
Sensory; pin prick	-	1	-	-
Mini-mental State (≤24 points)	-	-	-	-

No significant difference is found in comparison of the study groups (chi-square test).

TABLE VII

Comparison of the Mean Response of Laboratory Results Among the Three Study Matched Triads

Laboratory Test	Mean Response				Analysis of Variance - F statistic	P Value
	PBB Workers (n=36)	Electricians & Others (n=36)	Steel Workers & Others (n=36)	Total (n=108)		
Hematology						
Hemoglobin	15.60	15.30	15.61	15.50	1.356	0.26
Hematocrit	44.08	43.40	44.14	43.90	0.679	0.51
RBC	4.92	4.90	5.00	4.93	0.248	0.78
MCV	89.70	88.60	89.10	89.10	0.396	0.67
MCH	31.81	31.30	31.60	31.60	0.630	0.53
MCHC	35.40	35.10	35.30	35.23	1.068	0.35
Leucocytes	7.18	7.48	7.44	7.37	0.246	0.78
Neutrophils	53.11	54.80	49.64	52.51	2.584	0.08
Band	5.03	4.82	6.41	5.44	2.328	0.10
Eosinophils*	2.14	2.59	2.80	2.52	1.088	0.34
Basophils*	1.53	1.40	1.30	1.42	0.357	0.70
Monocytes	6.31	7.11	6.81	6.74	0.567	0.57
Lymphocytes	33.60	31.33	34.83	33.24	1.293	0.28

TABLE VII (continued)

Comparison of the Mean Response of Laboratory Results Among the Three Study Matched Triads

Laboratory Test	Mean Response				Analysis of Variance - F statistic	P Value
	PBB Workers (n=36)	Electricians & Others (n=36)	Steel Workers & Others (n=36)	Total (n=108)		
Blood Chemistry						
Sodium	141.50	140.40	141.30	141.10	1.416	0.25
Potassium	4.30	4.13	4.23	4.21	1.337	0.27
Chloride	102.81	101.64	102.61	102.35	1.419	0.25
CO_2	24.11	24.03	24.08	24.07	0.018	0.98
Blood Urea Nitrogen	15.69	15.94	15.20	15.60	0.362	0.70
Creatinine	1.13	1.14	1.11	1.13	0.263	0.77
Glucose	87.08	86.14	82.81	85.34	0.427	0.65
Calcium	10.08	10.20	10.00	10.10	1.501	0.23
Phosphorus	3.32	3.70	3.44	3.50	3.491	0.03
Total Protein	7.95	7.90	7.90	7.90	0.423	0.66
Uric Acid	5.71	5.83	6.04	5.90	0.522	0.59
Acid Phosphatase	2.83	2.71	2.81	2.80	0.575	0.56
Cholesterol	188.60	191.90	187.40	189.30	0.175	0.34

TABLE VII (continued)

Comparison of the Mean Response of Laboratory Results Among the Three Study Matched Triads

Laboratory Test	Mean Response					Analysis of Variance - F statistic	P Value
	PBB (n=36)	Electricians & Others (n=36)	Steel Workers & Others (n=36)	Others (n=30)	Total (n-138)		
Endocrine							
Testosterone	653.3	613.3	708.4	-	659.3	1.590	0.21
FSH	5.83	6.19	6.03	7.97	6.43	1.122	0.34
log FSH	0.66	0.71	0.72	0.73	0.70	0.332	0.80
LH	10.12	8.81	9.46	10.84	9.76	0.417	0.74
log LH	0.88	0.89	0.90	0.89	0.89	0.353	0.99
T4	7.72	8.45	8.10	-	8.10	0.861	0.43
TSH	6.08	1.87	2.07	2.04	3.06	3.755	0.01
log TSH	0.41	0.24	0.27	0.26	0.30	2.566	0.06
RUR	0.94	0.94	1.0	-	0.94	0.588	0.56
FTI	7.20	7.80	7.63	-	7.52	0.880	0.42

TABLE VII (continued)

Comparison of the Mean Response of Laboratory Results Among the Three Matched Study Triads

Laboratory Test	Mean Response				Analysis of Variance - F statistic	P Value
	PBB Workers (n=36)	Electricians & Others (n=36)	Steel Workers & Others (n=36)	Total (n=108)		
Urine						
Spot Urine						
Creatinine	1058.61	1034.44	993.61	1028.89	0.076	0.93
Δaminolevulinic acid	2.22	2.40	2.20	2.30	0.150	0.86
Porphobilinogen	0.80	0.90	0.80	0.80	0.331	0.72
Coproporphyrin	96.50	95.42	87.80	93.22	0.180	0.83
Uroporphyrin	10.10	9.30	10.92	10.10	0.427	0.65
24 hour Urine	(27 cases)	(11 cases)	(17 cases)	(55 cases)		
Creatinine	1157.20	1368.64	1114.40	1186.24	0.681	0.51
δ aminolevulinic acid	2.64	3.00	2.80	2.75	0.272	0.76
Porphobilinogen	0.70	0.92	0.72	0.73	1.108	0.34
Corproporphyrin	68.04	76.10	81.41	73.80	0.480	0.62
Uroporphyrin	11.50	14.10	13.90	12.74	0.977	0.38

*See log-response for better comparison.

TABLE VII (continued)

Comparison of the Mean Response of Laboratory Results Among the Three Study Matched Triads

Laboratory Test	Mean Response				Analysis of Variance - F statistic	P Value
	PBB Workers (n=36)	Electricians & Others (n=36)	Steel Workers & Others (n=36)	Total (n=108)		
Blood Chemistry (cont.)						
Total Bilirubin	0.50	0.34	0.40	0.40	1.676	0.19
SGPT	20.30	23.81	21.70	21.92	0.877	0.42
γGT	32.72	41.36	36.14	36.74	0.260	0.77
LDH	285.80	283.22	282.14	283.70	0.019	0.98
Albumin	5.14	5.10	5.00	5.07	2.076	0.13
Globulin	2.81	2.82	2.90	2.83	0.282	0.75
Albumin Globulin Ratio	1.90	1.82	1.81	1.83	0.486	0.62
SGOT	22.94	27.00	26.64	25.52	0.570	0.57
Alkaline Phosphatase	24.08	27.20	24.20	25.16	1.150	0.32
Triglycerides	2.08	2.30	1.80	2.05	0.977	0.38

TABLE VII (cont)

Comparison of the Mean Response of Laboratory Results Among the Three Study Matched Triads

Nerve Conduction Velocity*	Mean Response PBB Workers	Electricians and Others	Steel Workers and Others	Total	Analysis of Variance - F statistic	P Value
Median Motor	56.78 (32)	56.45 (28)	59.01 (33)	57.47 (93)	2.02	.1381
Peroneal Motor	45.36 (32)	44.80 (29)	47.43 (32)	45.90 (93)	3.39	.0381
Median Sensory	55.09 (34)	54.33 (29)	53.87 (33)	54.44 (96)	.421	.6574
Ulnar Sensory	51.04 (33)	50.78 (27)	50.14 (28)	50.68 (88)	.186	.8306
Sural Sensory	43.96 (33)	48.77 (30)	45.88 (33)	46.12 (96)	4.68	.0116
Log Sural Sensory	1.64 (33)	1.685 (30)	1.657 (33)	1.66 (96)	4.95	.0090

*The triads are not age-matched (note reduced number of subjects in ()) due to velocities not available, e.g., subject requested no testing. This table is presented in the interest of completeness, i.e., to offer a comparison across study triads on nerve conduction velocities. The reader is referred to Page 57 for the results of comparing across "pure" occupational groups, after subjects with all known extraneous causes for neurotoxicity have been excluded, and age-adjustment is attempted via analysis of covariance.

TABLE VIII

Percentage Distribution of Laboratory Results: Below, Within and Above Normal Range
Group Comparison of 108 Persons Included in the Age-Matched Triads

Laboratory Test	Low Levels			Normal			High Levels			Low	Normal	High	Chi	Sig.
	PBB	E	S	PBB	E	S	PBB	E	S	Total 108 Persons			Square	Level
Hematology														
Hgb.	5.6	11.1	2.8	94.4	88.9	97.2	-	-	-	6.5	93.5	-	2.13	0.34
Hct.	-	-	-	100.0	100.0	100.0	-	-	-	-	100.0	-	-	-
RBC	19.4	8.3	13.9	80.6	88.9	86.1	-	2.8	-	13.9	85.2	0.9	3.75	0.44
MCV	2.8	2.8	2.8	94.4	97.2	07.2	2.8	-	-	2.8	96.3	0.9	2.01	0.73
MCH	-	2.8	2.8	97.2	94.4	97.2	2.8	2.8	-	1.9	96.3	1.9	2.01	0.73
MCHC	-	-	-	97.2	100.0	97.2	2.8	-	2.8	-	98.1	1.9	1.01	0.60
Leucocyte	11.1	2.8	2.8	80.6	88.9	86.1	8.3	8.3	11.1	5.6	85.2	9.3	3.35	0.50
Neutrophil	8.3	11.1	11.1	69.4	58.3	77.8	22.2	30.6	11.1	10.2	68.5	21.3	4.39	0.35
Band	-	-	-	66.7	69.4	50.0	33.3	30.6	50.0	-	62.0	38.0	3.38	0.18
Eosinophil	19.4	11.1	11.1	80.6	83.3	80.6	-	5.6	8.3	13.9	81.5	4.6	4.02	0.40
Basophil	-	-	-	86.1	86.1	91.7	13.9	13.9	8.3	-	88.0	12.0	0.69	0.70
Monocyte	16.7	13.9	19.4	69.4	52.8	52.8	13.9	33.3	27.8	16.7	58.3	25.0	4.36	0.35
Lymphocyte	8.3	11.1	-	69.4	75.0	77.8	22.2	13.9	22.2	6.5	74.1	19.4	4.74	0.31

Key to Abbreviations: PBB, Polybrominated Biphenyl Workers; E, Electricians & Others; S, Steel Workers & Others; NA, Not Applicable; -, No Cases.

TABLE VIII (continued)

Percentage Distribution of Laboratory Results: Below, Within and Above Normal Range
Group Comparison of 108 Persons Included in the Age-Matched Triads

Laboratory Test	Low Levels			Normal			High Levels			Low	Normal	High	Chi	Sig.
	PBB	E	S	PBB	E	S	PBB	E	S	Total 108 Persons			Square	Level
Blood Chemistry														
Sodium	-	13.9	2.8	100.0	83.3	97.2	-	2.8	-	5.6	93.5	0.9	9.61	0.04
Potassium	-	-	-	100.0	100.0	100.0	-	-	-	-	100.0	-	-	-
Chloride	2.8	5.6	-	97.2	94.4	100.0	-	-	-	2.8	97.2	-	2.05	0.35
CO_2	44.4	41.7	33.3	55.6	58.3	66.7	-	-	-	39.8	60.2	-	1.00	0.60
Blood Urea Nitrogen	2.8	8.3	-	80.6	77.8	91.7	16.7	13.9	8.3	3.7	83.3	13.0	4.96	0.29
Creatinine	-	-	-	94.4	97.2	100.0	5.6	2.8	-	-	97.2	2.8	2.05	0.35
Glucose	-	2.8	-	94.4	94.4	100.0	5.6	2.8	-	0.9	96.3	2.8	4.07	0.39
Calcium	-	-	-	91.7	86.1	91.7	8.3	13.9	8.3	-	89.8	10.2	0.80	0.66
Phosphorus	2.8	-	5.6	07.2	83.3	91.7	-	16.7	2.8	2.8	90.7	6.5	11.24	0.02
Total Protein	-	-	-	8.3	25.0	13.9	91.7	75.0	86.1	-	15.7	84.3	3.90	0.14
Uric Acid	-	-	-	88.9	97.2	91.7	11.1	2.8	8.3	-	92.6	7.4	1.89	0.38
Acid Phosphatase	-	5.6	-	100.0	94.4	100.0	-	-	-	1.9	--	-	-	-
Cholesterol	-	-	-	-	-	-	-	-	-	-	-	-	-	-

TABLE VIII (continued)

Percentage Distribution of the Laboratory Results: Below, Within and Above Normal Range
Group Comparison of 108 Persons Included in the Age-Matched Triads

Laboratory Test	Low Levels			Normal			High Levels			Low	Normal	High	Chi Square	Sig. Level
	PBB	E	S	PBB	E	S	PBB	E	S	Total 108 Persons				
Blood Chemistry (cont.)														
Total Bilirubin	2.8	22.2	11.1	94.4	77.8	88.9	2.8	-	-	12.0	87.0	0.9	8.29	0.81
SGPT	—	—	—	83.3	75.0	88.9	16.7	25.0	11.1	-	82.4	17.6	2.43	0.30
γGT	-	-	-	86.1	77.8	83.3	13.9	22.2	16.7	-	82.4	17.6	0.89	0.64
LDH	-	-	-	52.8	50.0	52.8	47.2	50.0	47.2	-	51.9	48.1	0.07	0.96
Albumin	-	-	-	13.9	30.6	19.4	86.1	69.4	80.6	-	21.3	78.7	3.09	0.21
Globulin	-	-	-	97.2	100.0	91.7	2.8	-	8.3	-	96.3	3.7	3.63	0.16
Albumin Globulin Ratio	-	-	-	-	-	-	-	-	-	-	-	-	-	-
SGOT	-	-	-	88.9	83.3	86.1	11.1	16.7	13.9	-	86.1	13.9	0.46	0.79
Alkaline Phosphatase	-	-	-	100.0	97.2	100.0	-	2.8	-	-	99.1	0.9	2.02	0.36
Triglycerides	-	-	-	-	-	-	-	-	-	-	-	-	-	-

TABLE VIII (continued)

Percentage Distribution of the Laboratory Results: Below, Within and Above the Normal Range
Group Comparison of 108 Persons Included in the Age-Matched Triads

Laboratory Test	Low Levels			Normal			High Levels			Low	Normal	High	Chi Square	Sig. Level
	PBB	E	S	PBB	E	S	PBB	E	S	Total 108 Persons				
Endocrine														
Testosterone	-	-	-	100.0	100.0	97.2	-	-	2.8	-	99.1	0.9	1.96	0.37
FSH	NA	NA	NA	91.7	94.4	100.0	8.3	5.6	-	NA	95.4	4.6	2.93	0.23
LH	NA	NA	NA	86.1	94.4	88.9	13.9	5.6	11.1	NA	89.8	10.2	1.41	0.49
T_4	8.3	5.6	5.6	77.8	91.7	88.9	13.9	2.8	5.6	6.5	86.1	7.4	3.98	0.40
TSH	NA	NA	NA	86.1	97.2	100.0	13.9	2.8	-	NA	94.4	5.6	7.41	0.02
RUR	8.3	16.7	13.9	91.7	80.6	86.1	-	2.8	-	13.0	86.1	0.9	3.25	0.51
FTI	8.3	2.8	-	83.3	91.7	94.4	8.3	5.6	5.6	3.7	89.8	6.5	4.05	0.39
Urine-24 hour														
D-Amino Acid	7.4	9.1	5.9	92.6	90.9	88.2	-	-	5.9	7.3	90.9	1.8	2.35	0.67
Porphobilinogen	-	-	-	96.3	100.0	94.1	3.7	-	5.9	-	96.4	3.6	0.66	0.71
Corphoporphyrin	29.6	18.2	11.8	70.4	81.8	88.2	-	-	-	21.8	78.2	-	2.05	0.35
Uroporphyrin	66.7	45.5	41.2	33.3	54.5	58.8	-	-	-	54.5	45.5	-	3.19	0.20

TABLE IX

Percentage Distribution of Laboratory Results: Below, Within and Above Normal Range for Entire Study Population

Lab. Test	Negative				Trace				+				++				Neg.	Trace	+	++	Chi Square	Sig. Levels
	PBB (n=36)	E (n=36)	S (n=36)	O (n=30)	PBB (n=36)	E (n=36)	S (n=36)	O (n=30)	PBB (n=36)	E (n=36)	S (n=36)	O (n=30)	PBB (n=36)	E (n=36)	S (n=36)	O (n=30)	Totals (138 persons)					
Urine Dipstick of Spot Urines																						
Nitrate	86.1	100.0	91.7	83.3	-	-	-	-	13.9	-	8.3	16.7	-	-	-	-	90.6	-	9.4	-	6.48	0.09
ph	-	-	-	-	-	-	-	-	100.0	100.0	100.0	100.0	-	-	-	-	-	-	100.0	-	-	-
Protein	30.6	30.6	30.6	46.7	66.7	63.9	66.7	46.7	2.8	5.6	-	6.7	-	-	2.8	-	34.1	61.6	3.6	0.7	8.55	0.47
Glucose	91.7	97.2	97.2	96.7	5.6	-	-	-	2.8	-	2.8	-	-	2.8	-	3.3	95.7	1.4	1.4	1.4	9.79	0.36
Ketones	88.9	88.9	97.2	83.3	-	-	-	3.3	5.6	8.3	-	13.3	5.6	2.8	2.8	-	89.9	0.7	6.5	2.9	10.43	0.11
Blood	94.4	88.9	91.7	83.3	2.8	8.3	5.6	-	2.8	2.8	-	10.0	-	-	2.8	6.7	89.9	4.3	3.6	2.2	12.41	0.19

Key to Abbreviations: PBB, Polybrominated Biphenyl Workers; E, Electricians; S, Steel Workers; O, Others including 2 "unmatched" electricians; -, No Cases.

TABLE X

Correlation Between Laboratory Variables and Length of Employment of 36 PBB Workers (Male)

Test	r	Test	r
Blood Chemistry		**Endocrine**	
Sodium	-0.201	Testosterone	0.377
Potassium	-0.195	FSH	0.336
Chloride	-0.021	T_4	0.096
CO_2	0.103	FTI	0.047
Blood urea nitrogen	-0.199	LH	0.389
Creatinine	-0.074	TSH	0.042
Glucose	-0.089	RUR	0.127
Calcium	-0.158		
Phosphorus	-0.129		
Total Protein	-0.319	**Hematology**	
Uric Acid	-0.197		
Acid phosphatase	0.008	Hemoglobin	0.138
Cholesterol	0.040	Hematocrit	0.120
Bilirubin	-0.177	RBC	0.174
SGPT	0.125	MCVC	0.168
γGT	-0.085	MCH	0.142
LDH	0.21	MCHC	0.081
Albumin	-0.127	Leucocytes	0.123
Globulin	-0.221	Neutrophils	0.058
A/G ratio	0.137	Band	0.110
SGOT	-0.021	Eosinophil	0.272
Alkaline phosphase	-0.090	Basophil	0.491
Triglycerides	-0.290	Monocytes	0.011
		Lymphocytes	0.079

$|r| = 0.275, 0.325, 0.381$ are the 0.10, 0.05, and 0.02 percentage points (respectively, with 35 degrees of freedom) of the correlation coefficient under the null hypothesis of no correlation, i.e., $\zeta=0$.

TABLE XI

Medical, Drinking and Smoking History of Persons with Elevated Liver Function Tests[1]

Occupational Group / Case	Age	Sex	Abnormal Liver Function Tests γGT	SGPT	SGOT	Bili-rubin	LDH	Alk P	Other data from laboratory, medical history or physical examination	Use of Drugs	Alcohol Use per week[2] B	W	Md	Smoking History PPD[3]	Yrs.
PBB Workers															
1	51	M	X						cirrhosis of liver, ↑BP, kidney stones, present ↑TSH		Heavy in past			1½	38
2	26	M	X						bromide fumes in eyes		24	-	occ.	1	7
3	26	M				X					2	-	-	1	2
4	58	M					X		malaria, MI, shingles	aspirin, Tolinase	1	-	-	pipe, 6-8	
5	31	M		X	X		X		ex-heroin addict	Methadone	14	-	-	1	7
Electricians															
6	43	M		X							48	10	-	3	22
7	27	M		X					hip fract., pneumonia		2	1-2	-	1½	8
8	48	M	X		X				glomerulonephitis, pneumonia		-	6	2	2	25
9	56	M	X	X	X			X	lymphoma	radiation Compazine	4	-	3	1	3
Steel Workers															
10	23	M	X								100	-	20	1	5
11	61	M		X					hemorrhoids, hernia		-	-	-	-	-
12[4]	30	M	X	X	X		X		serum hepatitis, bronchitis, asthma	Bronkade	42	-	-	1	13
13[4]	27	F	X	X		X	X		chronic hepatitis (serum hepatitis)		3[5]	3[5]	6[5]	2	8

[1] γGT >75 μ/1; SGPT >42 μ/1; SGOT >595 μ/1; Bilirubin >1.275 mg/dl; LDH >375 μ/1; Alkaline Phosphatase >45.5 μ/1.
[2] B, cans of beer; W, glasses of wine; Md, mixed drinks.
[3] PPD, packs of cigarettes per day.
[4] Cases 12 and 13 are husband and wife.

TABLE XII A

Total PBB's Serum Levels by Occupational Group

Results	PBB Workers No.	%	Electricians No.	%	Steel Workers No.	%	Others No.	%	Total No.	%
Not detectable	13	33.3	20	47.6	13	50.0	16	53.3	62	45.3
Not confirmed*	9	23.1	14	33.3	7	26.9	11	36.7	41	29.9
Trace**	3	7.7	3	7.1	2	7.7	0	0.0	8	5.8
Detectable level	14[1]	35.9	5[2]	11.9	4[3]	15.4	3[4]	10.0	26	19.0
Not available	0	-	0	-	0	-	1	-	1	-
Total	39	100.0	42	99.9	26	100.0	31	100.0	138	100.0

* Not confirmed = impossible to confirm any detectable level. For most practical purposes, equivalent to "not detectable".

** Trace = below measurable level

"-" Not included in the total

[1] Serum levels of PBB workers: .5, 2.4, 12.0, 15.0, 20.0, 20.5, 29.0, 40.4, 50.0, 58.0, 94.0, 132.3, 318.0, 1340.0 (ng/mL)

[2] Serum levels of electricians: .4, 1.9, 2.0, 4.0, 6.0 (ng/mL)

[3] Serum levels of steel workers: .3, 1.5, 2.2, 7.8 (ng/mL)

[4] Serum levels of others: 2.2, 5.5, 13.0 (ng/mL)

REMARK: A significantly higher number of PBB workers had a detectable level of PBBs as compared with other workers in the study (35.9 percent as compared to 12.2 percent, chi square = 8.67, $p<0.005$). Among workers with detectable PBB levels, the PBB workers had significantly higher serum levels ($p<0.001$) as compared to other workers ($Z = 3.61$, Mann-Whitney U test).

TABLE XII B (continued)

Total PBBO's Serum Levels by Occupational Group

Results	PBB workers No.	%	Electricians No.	%	Steel Workers No.	%	Others No.	%	Total No.	%
Not detectable	14	35.9	8	20.0	6	24.0	10	37.0	38	29.0
Not confirmed*	6	15.4	10	25.0	8	32.0	7	25.9	31	23.7
Trace**	7	17.9	6	15.0	6	24.0	4	14.8	23	17.6
Detectable level	12[1]	30.8	16[2]	40.0	5[3]	20.0	6[4]	22.2	39	29.8
Not available	0	-	2	-	1	-	4	-	7	-
Total	39	100.0	42	100.0	26	100.0	31	99.9	138	100.1

* Not confirmed = impossible to confirm any detectable level. For most practical purposes equivalent to "not detectable".

** Trace = below measurable level

"-" Not included in the total

[1]Serum levels of PBB workers: .2, .4, .5, .6, .8, .9, 1.3, 2.3, 2.4, 2.7, 5.2, 5.2 (ng/mL)

[2]Serum levels of electricians: .4, .5., .7, .8, .8, .8, .9., 1.0, 1.0, 1.3, 1.6, 1.6, 2.0, 3.1, 3.7, 4.0 (ng/mL)

[3]Serum levels of steel workers: .3, .6, .6, 1.8, 2.1, 2.5 (ng/mL)

[4]Serum levels of others: .7, .8, .9, 1.9, 2.8 (ng/mL)

TABLE XII C (contined)

Total PCB's Serum Levels by Occupational Group

Results	PBB workers		Electricians		Steel Workers		Others		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
Not detectable	2	5.1	1	2.5	0	0.0	0	0.0	3	2.3
Not confirmed*	3	7.7	2	5.0	1	4.0	4	14.8	10	7.6
Detectable level	34[1]	87.2	37[2]	92.5	24[3]	96.0	23[4]	85.2	118	90.1
Not available	0	-	2	-	1	-	4	-	7	-
Total	39	100.0	42	100.0	26	100.0	31	100.0	138	100.0

* Not confirmed = impossible to confirm any detectable level. For most practical purposes equivalent to "not detectable"

"-" Not included in the total

[1] The 4 highest levels of PBB workers: 74.7, 71.2, 31.7, 30.4 (ng/mL)

[2] The 4 highest levels of electricians: 5,321.8, 349.0, 77.3, 34.0 (ng/mL)

[3] The 3 highest levels of steel workers: 49.6, 41.7, 40.4 (ng/mL)

[4] The 3 highest levels of others: 33,000, 194.0, 31.8 (ng/mL)

TABLE XIII

Detectable* Serum Levels of PBBs, PBBOs and PCBs (ng/mL)
(38 Samples Analyzed)

Polybrominated Biphenyls (PBBs)				Polybrominated Biphenyl Oxide (PBBOs)				Polychlorinated Biphenyls (PCBs)			
	No.	Minimum	Maximum		No.	Minimum	Maximum		No.	Minimum	Maximum
$C_{12}H_9Br$	14	0.3	5.5	$C_{12}H_9BrO$	36	0.2	3.1	$C_{12}H_9Cl$	9	0.6	14.0
$C_{12}H_8Br_2$	1	6.9	6.9	$C_{12}H_8Br_2O$	0	-	-	$C_{12}H_8Cl_2$	10	0.3	2.3
$C_{12}H_7Br_3$	1	0.9	0.9	$C_{12}H_7Br_3O$	8	0.8	4.7	$C_{12}H_7Cl_3$	48	0.2	240.0
$C_{12}H_6Br_4$	0	-	-	$C_{12}H_6Br_4O$	0	-	-	$C_{12}H_6Cl_4$	101	0.3	7,600.0
$C_{12}H_5Br_5$	2	1.6	13.0	$C_{12}H_5Br_5O$	0	-	-	$C_{12}H_5Cl_5$	103	1.0	20,000.0
$C_{12}H_4Br_6$	2	0.4	6.0	$C_{12}H_4Br_6O$	0	-	-	$C_{12}H_4Cl_6$	105	0.6	4,900.0
$C_{12}H_3Br_7$	7	9.0	40.0	$C_{12}H_3Br_7O$	0	-	-	$C_{12}H_3Cl_7$	54	0.3	200.0
$C_{12}H_2Br_8$	9	20.0	800.0	$C_{12}H_2Br_8O$	0	-	-	$C_{12}H_2Cl_8$	1	27.0	27.0
$C_{12}HBr_9$	1	500.0	500.0	$C_{12}HBr_9O$	0	-	-	$C_{12}HCl_9$	0	-	-
$C_{12}Br_{10}$	0	-	-	$C_{12}Br_{10}O$	0	-	-				
Total PBBs	26	0.3	1,340.0	Total PBBOs	39	0.2	5.2	Total PCBs	115	1.0	33,000.0

*Excludes cases with "trace", "not detectable" or "not confirmed" levels, and cases where sera were "not available" for testing

Table XIV

Selected Characteristics and Cause of Death for Decedent PBB Workers

	Worker A	Worker B	Worker C	Worker D
Age	54	63	59	56
Occupation	Chemical operator	Maintenance	Chemical operator	Maintenance
Dates of Employment	11/7/69 to 1/4/76	5/20/71 to 4/4/76	2/30/70 to 5/15/78	2/26/69 to 12/2/77
Dates of Death	1/4/76	4/4/76	5/16/78	12/2/77
Immediate Cause of Death	Acute myocardial infarction due to coronary sclerosis	metastatic bronchogenic carcinoma	electrolyte imbalance due to peritomitis, associated with massive arcites due to partial cirrhosis	metastatic lung cancer
Contributing Cause of Death	von Reckling-hausen's disease	--	diabetes mellitus, arterio-sclerotic heart disease	--
Autopsy	No	No	Yes	--

Because a total of only four known deaths has occurred, a meaningful comparison could not be made with expected deaths. However, it should be noted that all workers died at relatively young ages. Two workers died of the cancer of the respiratory system, a disease often cited as occupational risk in a chemical dust-filled environment, and two workers had heart disease. Although there is no way to determine whether these workers had a thyroid dysfunction, it is recognized that hypothyroidism can lead to atherosclerotic heart disease.